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ASSOCIATION OF KERATOMALACIA WITH OTHER DEFICIENCY DISEASES *

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The study of diseases in man due to the lack of various essential dietary constituents is still far from complete. The results of feeding experiments with animals have helped to define the rôle of an ever increasing number of vitamins and have served to focus attention on the most conspicuous manifestations of individual deficiency diseases in man. But, as Keefer and Yang [1] have recently emphasized, the exact methods of the laboratory are not obtainable with observations on human disease. The diet of the experimental animal is chosen with meticulous care; that of the human being is dictated by geographic location, class or racial custom, individual appetite and the exigencies of economy. A diet so limited as to be deficient in one essential is liable to be defective in several. It is true that the resulting disease may be dominated by symptoms pointing to the absence of one definite constituent, but it must be emphasized that the greatest care is necessary in interpreting minor symptoms as due to the same deficiency that causes the major one merely because they appear concomitantly in the same patient or even in a group of patients. In China the diet of the average person is so close to threshold requirements in several important constituents that deficiency diseases are extremely common and constitute one of the major groups of conditions with which the physician has to deal. H. Wu and D. Y. Wu [2] have pointed out that the diet of the average Chinese contains a suboptimal amount of protein and a relatively small amount of fat, practically all of which is of vegetable origin. As a result, it is often deficient in vitamins A and D. The quantities of vitamins B and C are usually adequate, although the danger of deficiency in vitamin B is not entirely absent. The diet is also low in calcium and phosphorus.

The results are plainly seen in patients who come to the hospitals for treatment. Keratomalacia is extremely widespread in China both in

* Submitted for publication, Dec. 31, 1929.

* From the Division of Pediatrics of the Department of Medicine, Peiping Union Medical College.

1. Keefer, C. S., and Yang, C. S.: The Rôle of the Various Vitamins in the Production of Anemia, Nat. M. J. China **15**:419, 1929.

2. Wu, H., and Wu, D. Y.: Study of Dietaries in Peking, Chinese J. Physiol., rep. ser. **1**:135 (July) 1928.

children [3] and in adults.[4] Beriberi is not infrequently encountered.[5] Rickets, although distinctly less common than in many American cities, is not rare [6] and its counterpart in the adult, osteomalacia, is unusually prevalent in some localities.[7] In addition one sees frequent examples of so-called edema disease, the etiology of which condition, although obscure, is certainly related to faulty nutrition. On the other hand, scurvy is rarely met with, a fact undoubtedly due to widespread inclusion of cabbage (rich in vitamin C) [8] in the dietary. Not only are the deficieny diseases here mentioned extremely prevalent, but it is becoming increasingly apparent, as might be expected, that evidence of multiple deficiency disease is frequently presented by the same patient. Indeed, the association has been noted so often in this clinic that many regard it as imperative to look with particular care for evidences of all the deficiency diseases in any patient who presents symptoms of one. A recent case illustrating the importance of this may be cited. The patient, an infant, was admitted for treatment for active rickets. A casual examination of the eyes led to the conclusion that they were normal. Fortunately, cod liver oil was administered for the rickets. As the rickets healed, bilateral corneal scars appeared, indicating the healing of an associated keratomalacia. Had some other antirachitic agent been employed, ultraviolet light or viosterol, the effect on the eyes could not have been so fortunate.

The present study began with an attempt to demonstrate an associated lack of vitamin D in patients with keratomalacia who, therefore, were known to be suffering from a deprivation of vitamin A. The association seemed likely, as both of the vitamins are fat-soluble and usually occur together. In the course of the study, several other associations which will be discussed came to light. The observations were made on

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3. Hsu, K. L.: Nutritional Keratomalacia: Report of Cases, China M. J. **41**:825 (Oct.) 1927.

4. Pillat, A.: The Frequency of Deficiency Diseases of the Eye Due to Lack of Vitamin A in a Military Camp North of Peiping, Nat. M. J. China **15**:585, 1929; Does Keratomalacia Exist in Adults? Arch. Ophth. **2**:256 (Sept.) 1929 and 399 (Oct.) 1929.

5. Statistics concerning the incidence of beriberi in China have not been available to the author. It is generally known to be more prevalent in south China where rice forms the staple article of most diets than in the north. The records at the Peiping Union Medical College hospital disclose a diagnosis of this disease seventy-three times among a total of 26,000 admissions. This represents an incidence of approximately 0.3 per cent among all hospital patients.

6. Tso, E.: Incidence of Rickets in Peking: Efficacy of Treatment with Cod-Liver Oil, China M. J. **38**:112 (Feb.) 1924.

7. Maxwell, J. P., and Miles, L. M.: Osteomalacia in China, J. Obst. & Gynaec. Brit. Emp. **32**:433, 1925.

8. Tso, E.: The Anti-Scorbutic Vitamin in Cabbage Soup, Cabbage Puree and Turnip Juice, Chinese J. Physiol. **2**:403 (Oct.) 1928.

thirteen children with keratomalacia, all under the age of 3½ years. With the exception of one case, that of a patient who died the day following admission, the diagnosis of keratomalacia was in every instance confirmed by Dr. A. Pillat of the department of ophthalmology of the Peiping Union Medical College or by a competent member of his department, and included microscopic examination of scrapings from the cornea.[9]

ASSOCIATION OF RICKETS WITH KERATOMALACIA

In ten of the thirteen cases, analyses of the blood serum for calcium and inorganic phosphorus or roentgenograms of the extremities, or both, were made to determine the presence or absence of rickets. In interpreting the chemical analyses of the blood, the method of Howland and Kramer[10] was followed. These authors stated that when the product of calcium and inorganic phosphorus, expressed in milligrams per hundred cubic centimeters of blood serum, is less than 30, rickets is present, that when the product lies between 30 and 40, rickets may or may not be present, and that when the product is above 40, rickets is either absent or undergoing the process of healing.[11] In comparing the results of roentgen examinations with those obtained by analyses of blood serum, it should be borne in mind that the roentgenogram depicts the story of the past, whereas the chemistry of the blood indicates whether a rachitic process is active or absent at the time of examination. The bone changes in rickets require time for their production and are dependent on growth. In general, the observations by blood chemistry may be said to indicate a deficient or adequate supply of vitamin D at the time of examination.

The results with my cases have been listed in table 1. In each case the roentgenograms and blood for analysis were obtained within a few days of the time of admission and at a time when the keratomalacia was in an active stage. The table requires several words of explanation. In case 2, roentgenograms were not obtained, as the patient, who had recently recovered from measles, was being held in quarantine. In cases 4 and 10, death occurred within less than twenty-four hours after admission and before blood could be withdrawn for analysis. In these cases,

9. Pillat (footnote 4, second reference).

10. Howland, J., and Kramer, B.: Factors Concerned in Calcification of Bone, Tr. Am. Pediat. Soc. **34**:204, 1922.

11. The author is aware of theoretical objections to the simple Ca × P product made by Holt, La Mer and Chown (J. Biol. Chem. **64**:509 [July] 1925). These investigators stated that the ion product $(Ca^{++})^3 \times (PO_4^{\equiv})^2$ is a more accurate criterion of the rate of deposition of lime salts. The simpler expression is used here because experience has proved it to be trustworthy and because the whole question of the chemical factors involved in bone formation is still under dispute. Recently Shear and Kramer (Ibid. **79**:125 [Sept.] 1928) have presented new evidence in favor of the validity of the empiric Ca × P product.

the roentgenograms were obtained post mortem. In two instances the product of serum calcium and inorganic phosphorus lay in the equivocal zone between 30 and 40. In both instances, these were interpreted as nonrachitic because of the roentgen observations. The interpretation of the observations in case 13 requires special explanation. With this patient, roentgenograms of the extremities failed to reveal any signs of rickets, whereas the calcium-inorganic phosphorus product in the blood serum was only 27.8. The possibility of the divergence being due to error was excluded by repetition of the analyses and careful rechecking of the reagents used in the determinations.[12] The case was classified as nonrachitic both because of the roentgenograms and because the patient also presented a nutritional edema with a low value for blood

TABLE 1.—*Occurrence of Rickets in Present Series of Cases* *

Case	Age, Months	Seasonal Occurrence	Duration of Keratomalacia, Days	Roentgenologic Observations	Ca per 100 Cc. of Serum, Mg.	P per 100 Cc. of Serum, Mg.	Ca × P	Interpretation
1	36	Jan.	5	Rickets absent	9.0	3.9	35.1	No rickets
2	22	Feb.	15	.....	9.7	4.2	40.7	No rickets
3	6	March	?	Marked rickets	6.1	4.3	26.2	Rickets
4	30	April	?	Rickets absent	....	...	....	No rickets
5	3	May	12	Rickets	8.5	2.9	24.7	Rickets
8	16	July	0†	Marked rickets (healing)	9.7	5.4	52.4	Healing rickets
9	18	July	5	Marked rickets (healing)	10.5	5.5	57.8	Healing rickets
10	9	Aug.	14	Rickets (healing)	....	...	....	Healing rickets
12	3	Aug.	?	Rickets absent	9.2	3.8	35.0	No rickets
13	38	Oct.	16	Rickets absent	8.7	3.2	27.8	No rickets

* Studies made at once.
† Developed keratomalacia while in hospital.

serum protein. It is now known that the total amount of calcium in the blood varies with the protein as well as with the inorganic phosphorus. Only because the serum proteins are usually fairly constant is the simple relation between calcium and inorganic phosporus established by Howland and Kramer [10] generally true. With this patient the serum protein content was only 4.57 mg. per hundred cubic centimeters. Using this figure and the value for serum calcium obtained by analysis, I have calculated from the formula of Peters and Eiserson [13] the level of inorganic phosphorus to be expected if there were no primary disturbance of the calcium-phosphorus metabolism. This level is 3.47 mg. per hundred cubic centimeters. Actually, a value of 3.2 mg. was found by analysis. If the serum proteins had been normal in this case,

12. Calcium was determined by the Clark-Collip modification of the Kramer-Tisdall method (J. Biol. Chem. **63**:461 [March] 1925, inorganic phosphorus by the method of Fiske and Subbarow (Ibid. **66**:375 [Dec.] 1925).

13. Peters, J. P., and Eiserson, L.: The Influence of Protein and Inorganic Phosphorus on Serum Calcium, J. Biol. Chem. **84**:155 (Oct.) 1929.

that is, between 6.5 and 8.2 mg. per hundred cubic centimeters,[14] the expected level of inorganic phosporus would have been between 7.8 and 11.5 mg. per hundred cubic centimeters, and the observed value would have been extremely low. It is legitimate, therefore, in this instance to interpret the low calcium-inorganic phosphorus product in the blood serum as due to an unusually low level of protein in the blood and not to a coexisting rickets. As will be discussed later, several additional patients of the series also presented nutritional edema and probably would have shown low values for serum proteins if analyses had been made. It may be noted that such observations would in each instance have furnished stronger evidence in favor of the interpretations given and could not have invalidated them.

It will be observed that there were two patients who suffered from keratomalacia and rickets at the same time, three patients in whom previously active rickets was undergoing repair at a time when keratomalacia was active and five patients with keratomalacia but with no rickets.

Aside from demonstrating the fact that keratomalacia and rickets may coexist in man, it is interesting to inquire why not all of the children showed evidence of active rickets. The two fat-soluble vitamins, A and D, usually occur together and, unless exceptional precautions are taken, a diet so chosen as to be deficient in vitamin A will also be deficient in vitamin D. Several explanations suggest themselves. In the first place, it is well known that rickets cannot be produced experimentally in animals unless the diet is low not only in vitamin D but also in either calcium or phosphorus. To what extent a deficiency of lime salts is necessary for the development of rickets in the human being is much less clear since it is known that infants fed with cow's milk, which contains a considerably higher proportion of calcium and phosphorus than woman's milk, not infrequently develop rickets. Quite aside from this consideration, however, the suggestion that the Chinese child with keratomalacia has been protected against rickets because his diet contains optimal quantities of calcium and phosphorus seems untenable in view of the fact that it is known to be deficient in these elements.[2] Secondly, the results of feeding experiments with rats have demonstrated that a diet containing proteins of poor quality, in addition to a deficiency of vitamin A, will produce xerophthalmia more rapidly than one containing proteins of good quality.[15] In China the total quantity of protein in the average diet is not only less than in western countries but the bulk of what protein there is is derived from leguminous veget-

14. Hawk, P. B., and Bergeim, O.: Practical Physiological Chemistry, ed. 9, Philadelphia, P. Blakiston's Son & Company, 1927, p. 357.

15. Powers, Park and Simmonds (footnote 16, second reference, p. 578, note regarding diet 3392).

ables. For the needs of the animal organism this protein is known to be of poorer quality than that of animal origin. It seems highly probable, therefore, that protein deficiency may be a factor of importance in the high incidence of keratomalacia in China. That its importance is great enough to allow the production of disease of the eyes before an associated deficiency of vitamin D has had time to manifest itself seems doubtful.

The third and undoubtedly most important factor is the influence of sunlight. It is now known that by the action of sunlight the body is able to synthesize vitamin D in abundance but that vitamin A cannot be so generated.[16] In northern China the annual supply of sunshine is exceedingly abundant. The rainy season is of comparatively short duration (from six to eight weeks); during the remainder of the year the atmosphere for the most part is dry and clear. Even in the city, Peiping, the air is not clouded by the smoke of industrial factories as in many western cities. Moreover, the construction of the average Chinese house, with its open courtyard, favors a maximal exposure to the sun. During the summer the majority of young children are covered with scant clothing. Many are allowed to go naked. One might naturally expect these facts to be reflected in the incidence of rickets in general. They are to the extent that although the condition itself is not an uncommon disorder,[6] it is unusual to find examples of rickets of long duration accompanied by skeletal deformity. In most cases it is a disease of infants who have not passed through a summer in the sunlight. Two cases of marked thoracic deformity due to rickets have been observed in this ward in the past year. In both instances a history was obtained of confinement indoors, which was at first occasioned by illness and later continued because of weakness due to the rickets. Inasmuch as the dietary factors are distinctly at fault, it would seem that the paucity of rickets after the year of infancy must be attributed to the influence of sunlight. This supposition finds support in the cases reported here. In three instances (cases 8, 9 and 10) in which evidence of active bone regeneration (healing rickets) was found in association with keratomalacia, the disease of the eyes developed during the summer months. In three instances (cases 1, 2 and 4) in which keratomalacia occurred during the winter and spring months unassociated with rickets, the children were all so old as to have had the advantage of a previous summer's sunlight. That this advantage might have been sufficient to prevent rickets during the cold season of the year, even neglecting the influence of the winter sun, is suggested by an experi-

16. Bloch, C. E.: Light and the A-Body, Am. J. Dis. Child. **31**:315 (March) 1926. Powers, G. F.; Park, E. A., and Simmonds, N.: The Influence of Radiant Energy upon the Development of Xerophthalmia in Rats, J. Biol. Chem. **55**:575 (April) 1923.

ment of Gerstenberger and Hartman.[17] These investigators showed that in patients with rickets due to a low supply of phosphorus a single exposure to mercury vapor quartz lamp ultraviolet rays caused the development of healing which continued, in a moderate degree, for sixty-one days. It seems highly probable that many exposures to the sun during an entire summer may be able to protect a growing child from rickets for a much longer period of time. In two instances (cases 3 and 5) in which rickets and keratomalacia occurred together, the infants were so young and the diseases developed at such a season of the year that previous exposure to sunlight was most improbable.

It seems worth while to reflect on these observations in the light of the development of knowledge concerning rickets during the past few years. Less than a decade ago, in the report of the Medical Research Council, Mellanby [18] declared his belief in the identity of the antirachitic vitamin with fat-soluble A. His report was not accepted without dissension, and the same year McCollum and his collaborators [19] reported that cod liver oil that had been heated to 100 C. for from twelve to twenty hours and oxidized by having air blown through it retained its property of curing rats of rickets but was no longer able to cure them of xerophthalmia. Thus the identity of a distinct antirachitic vitamin was established. The separation of the vitamins, A and D, became even more clear with the accumulation of knowledge concerning the physiologic properties of utltraviolet rays. It has been demonstrated repeatedy that these rays are effective in the cure of rickets but cannot alleviate xerophthalmia. It is interesting to observe that in China, probably for many generations, an experiment on human subjects has been conducted on a gigantic scale from which the identity of the two vitamins might have been inferred. Rickets and keratomalacia may occur together but are not necessarily so associated and the former may be in the process of healing when the latter becomes active.

ASSOCIATION OF KERATOMALACIA WITH DEFICIENCY DISEASES OTHER THAN RICKETS

Beriberi.—Although beriberi is not a rare disease in north China it is observed far less frequently than either keratomalacia or rickets.

17. Gerstenberger, H. J., and Hartman, J. I.: Observations on Rachitic Spasmophilia and Low Calcium Rickets, Tr. Am. Pediat. Soc. **39**:51, 1927; Quartz Lamp Therapy in Human Rickets and Rachitic Spasmophilia, J. A. M. A. **92**:367 (Feb. 2) 1929.

18. Mellanby, E.: Experimental Rickets, Med. Research Council Special Report Series, no. 61, London, His Majesty's Stationery Office, 1921.

19. McCollum, E. V.; Simmonds, N.; Becker, J. E., and Shipley, P. G.: Studies on Experimental Rickets: XXI. An Experimental Demonstration of the Existence of a Vitamin Which Promotes Calcium Deposition, J. Biol. Chem. **53**: 293 (Aug.) 1922; Bull. Johns Hopkins Hosp. **33**:229 (June) 1922.

Cases of infantile beriberi of the type that is found so commonly in breast-fed infants in the Philippine Islands have not been observed in this children's ward. Neurologic examinations of the patients of this series have not revealed alterations in the reflexes sufficient to arouse the suspicion of a coexisting polyneuritis. It is well known, however, that in the infant the principal symptoms arising from a deprivation of vitamin B are cardiac in origin.[20] In these cases enlargement of the heart and especially of the right side of the heart can be demonstrated by both physicial and roentgen examination. In the patients of this series, I was unable by physicial examination to find any with definite cardiac hypertrophy. With one patient (case 3), however, a roentgenogram of the chest revealed moderate enlargement of the heart, which subsequent examinations, following the addition of yeast to the diet, indicated had decreased appreciably. The following is a brief résumé of the history of this patient.

REPORT OF CASE

No facts were available relating to the patient's history prior to her admission to the hospital on March 22, 1929. Several hours earlier she had been deserted at the door of a local orphanage. Her age was estimated at about 6 months. Examination revealed a markedly undernourished infant (4.7 Kg.) with evidence of advanced keratomalacia. The palpebral and bulbar conjunctivae of both eyes were markedly inflamed and there was marked pericorneal injection. The whole cornea of the right eye had sloughed off, leaving a protruding bluish black mass covered with purulent fibrinous exudate. The left cornea was perforated in three places. Craniotabes was easily demonstrated, but there were no other outspoken signs of rickets except as revealed by laboratory examination (table 1). A roentgenogram of the chest on March 26 disclosed moderate enlargement of the heart. Because of a suspicion that the enlargement might represent mild beriberi, powdered yeast (0.25 Gm. three times a day) was added to a diet which previously had consisted of a dried milk formula with the addition of 20 cc. of cod liver oil daily. The antiscorbutic vitamin was furnished in the form of cabbage water, 50 cc. three times a day.

From the standpoint of her deficiency disease, the patient's course in the hospital was one of steady improvement although several weeks elapsed before she began to make substantial gains in weight. An operation was performed on March 25 to remove the prolapsed portions of the right eyeball. Evidences of inflammation steadily subsided, and healing and scarring slowly progressed. The appearance of the eyes on April 25 is shown in figure 1. Roentgenograms of the extremities obtained three weeks after admission demonstrated that healing of the rickets was progressing rapidly; the craniotabes had disappeared. Blood serum withdrawn for analysis on April 11 disclosed 11.5 mg. of calcium and 5.3 mg. of inorganic phosphorus per hundred cubic centimeters, the product being 60.9. For purposes of comparison, a second roentgenogram of the chest was obtained on April 18. As it had not been practicable to obtain teleoroentgenograms with an infant of such small size, the conditions under which the first film was taken, that

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20. Andrews, V. L.: Infantile Beriberi, Philippine J. Sc. **7**:67 (April) 1912. Vedder, E. B.: Beriberi. Abt: Pediatrics, Philadelphia, W. B. Saunders Company, 1926, vol. 2, chap. 27, p. 815.

is, the position of the infant and the distance of the tube from the film, were exactly duplicated with the second. This film indicated an appreciable reduction in the size of the heart. The longitudinal diameter of the heart had decreased from 6.8 to 6.2 cm., and the transverse diameter from 6.6 to 6.2 cm. The cardiac area, measured with a planimeter, had decreased from 22.4 to 19.1 sq. cm., a reduction in size amounting to 14.7 per cent of the original area. The appearance of the heart at the time of the two examinations is shown in figure 2.

Fig. 1 (case 3).—Appearance of eyes thirty-four days after admission.

A B

Fig. 2 (case 3).—Reduction in size of heart following yeast therapy: appearance on (*A*) March 26, 1929, and (*B*) April 18, 1929.

It is of course not possible to say that the reduction in cardiac size in this patient was the result of furnishing vitamin B, which had previously been deficient in the diet. As the associated diseases from which she suffered are not known to produce alterations in the size of the heart, it is conceivable that the original enlargement was the result of mild beriberi.

Scurvy.—In none of the patients of this series was it possible to make a diagnosis of an associated scurvy. In two cases purpuric spots were present on the skin, and the etiology of the lesions remained obscure. However, there were no other manifestations pointing to scorbutic etiology. In fact, experience up to the present time would indicate that infantile scurvy is extremely rare in northern China. Among 26,000 admissions to the Peiping Union Medical College hospital since 1921, only one case in a native Chinese child has been observed. This patient also suffered from rickets, as shown by clinical and serologic examinations, but there was no evidence of keratomalacia. It is interesting to observe that her diet had consisted chiefly of rice and boiled milk, the latter a most unusual article of food in China.

Edema Disease.—It is not my purpose in this communication to discuss the etiology of the so-called edema disease, a condition also described under a variety of different names, Ödemkrankheit (edema disease), Kriegsödem (war edema), Lagerkrankheit (camp disease), epidemic dropsy and hunger edema. For a full discussion the reader is referred to the excellent review by Bürger.[21] All observers are agreed, however, that the condition is essentially nutritional in origin; it appears most frequently on a diet composed largely of starches, although opinion varies as to the relative importance of deficiencies in the protein, fat and salt components. Several authors[22] have called attention to the similarity or identity of edema disease with the "mehlnährschaden" of Czerny and Keller, a disturbance developing in infants fed exclusively on a diet containing a high proportion of carbohydrate. Whether the edema which appears in association with a number of the avitaminoses is a manifestation of the particular vitamin deficiency that characterizes the clinical picture or whether it is an expression of an associated but distinct nutritional disorder must for the present remain an open question. So-called wet beriberi is the most familiar example. Edema is also not infrequently observed in association with scurvy. Hess[23] has paraphrased the terminology of beriberi by speaking of "wet" scurvy. It is also known that fully developed mehlnährschaden may include in its symptomology, in addition to edema, keratomalacia

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21. Bürger, M.: Die Ödemkrankheit, Ergebn. d. nn. Med. u. Kinderh. **18**: 189, 1920.

22. Bürger (footnote 21). Schittenhelm, A., and Schlecht, H.: Ueber Ödemkrankheit mit hypotonischer Bradykardie, Berl. klin. Wchnschr. **55**:1138 (Dec. 2) 1918; Ueber die Ödemkrankheit: V. Die Pathogenese der Ödemkrankheit, Ztschr. f. d. ges. exper. Med. **9**:82, 1919. Hamburger, F.: Das Hungerödem der Säuglinge, München. med. Wchnschr. **68**:579 (May 13) 1921.

23. Hess, A. F.: Scurvy Past and Present, Philadelphia, J. B. Lippincott Company, 1920.

and spasmophilia.[24] Strangely enough, the edema disease itself in nonedematous forms has been described. Numerous authors speak of edema disease without edema (Ödemkrankheit ohne Ödeme), and Payne and Payne [25] write of wet and dry forms of edema disease. In China, keratomalacia is most frequently not associated with edema; not infrequently, however, it is. The edema disease is also fairly common as a separate disorder. I have therefore come to feel that the edema exhibited by patients with keratomalacia is not a manifestation of vitamin A deficiency but the expression of an associated nutritional disorder.

The observations on my patients are listed in table 2. It will be observed that five patients exhibited edema and eight did not, and also

TABLE 2.—*Other Observations in Present Series*

	Case	Degree of Malnutrition, per Cent	Edema	Red Blood Cells per Cm., Million	Blood Hemoglobin, per Cent	Diarrhea: Type	Diarrhea: Duration, Days	Comment
Winter and Spring	1	?	0	4.2	80	Stools normal	..	Bronchopneumonia
	2	?	0	5.3	58	Stools normal	..	Bronchopneumonia
	3	35	0	4.5	70	Stools normal	..	.....
	4	49	++	2.1	35	Stools normal	..	Pneumonia with empyema
	5	37	0	2.2	45	Stools normal	..	.....
Summer and Autumn	6	41	0	3.9	72	Non-dysenteric	36	Bronchopneumonia
	7	7	0	3.6	75	Stools normal	..	Patient aged 2 months; entirely breast fed; mother a strict vegetarian
	8	24	0	4.3	65	Dysentery *	47	.....
	9	43	++	4.3	80	Dysentery *	20	.....
	10	29	0	?	?	Non-dysenteric	23	Purpura
	11	50	+	7.2	134	Dysentery	60	Dehydrated
	12	44	++	3.4	71	Non-dysenteric	?	.....
	13	45	+	4.9	85	Dysentery *	129	Purpura

* Mannite-fermenting dysentery bacillus recovered from stools.

that edema was more frequent in the summer and autumn group than in the winter and spring group. The explanation of the seasonal preference exhibited by the edema is, I believe, to be found in the occurrence of diarrhea as a complication. The seasonal incidence of diarrhea in children, both dysenteric and nondysenteric in origin, is well known. The one patient (case 4) who presented edema during the spring season, unassociated with diarrhea, also had a severe anemia in association with pneumonia and empyema. The complicating factors are sufficient to occasion doubt concerning the purely dietary origin of the edema in this case. The remaining four patients with edema were all admitted during the summer and early autumn, and all presented the

24. Finkelstein, H.: Lehrbuch der Säuglingskrankheiten, Berlin, Julius Springer, 1921.

25. Payne, G. C., and Payne, F. K.: The Incidence of an Edema Disease Among Children in the Republic of Haiti, Am. J. Hyg. **7**:73 (Jan.) 1927.

symptom of diarrhea which, except in one case, was known to have been of longer duration than either the edema or the keratomalacia. This exception occurred in the case of a child with no history of antecedent diarrhea, but in whom diarrheal stools were observed following admission. It is true, of course, that patients with the edema disease who do not have diarrhea are not infrequently observed in this clinic, but the association of the two conditions is so frequently noted as to render it most probable that diarrhea can act as an inciting cause of a previously latent nutritional disease. This probability is supported by the fact that a high percentage of children with dysentery in China exhibit edema as a complication. The relation between edema disease and diarrhea has been noted many times in the literature. Against the point of view that edema may be a symptom of the same dietary defect that is responsible for the disease of the eyes and that develops only when provoked by a complicating diarrhea are the fact that two patients (cases 8 and 10) gave a history of long-standing diarrhea but showed no evidence of edema and the known fact that the majority of patients who present the combination of symptoms, diarrhea and edema, do not have keratomalacia.

Concerning the possibility suggested by Pillat,[26] that the diarrhea in some of these cases had its origin in alterations in the epithelium of the intestines, due to the deficiency in vitamin A which caused the keratomalacia, I have little data on which to base an opinion. The suggestion is well worth consideration. I do not believe, however, that because a diarrhea was relieved by cod liver oil therapy, it was necessarily caused by avitaminosis. It is equally easy to believe that improvement in the general resistance of the body brought about by relief from the deficiency disease may have enabled the patient to throw off a chronic infection of the intestines. With the patients of this series it will be observed that diarrhea did not occur in the five cases in the winter and spring group but that it was present in seven of the eight cases in the summer and autumn group. This seasonal incidence is suggestive of additional etiologic factors, presumably of the same type as those responsible for the summer diarrheas of infancy in general, although it is possible that the added factor in some cases is no more than summer heat. The stools of the patients of this series were nondystenteric in three instances, and dysenteric, i.e., they contained blood and mucus, in four instances. In three of the latter four cases, a mannite-fermenting dysentery bacillus was isolated from cultures of the stool.

Anemia.—The purely dietary origin of some cases of secondary anemia is now generally recognized. The milk anemia of infancy

26. Pillat, A.: The General Symptoms of Keratomalacia of Adults, China M. J. **43**:907 (Sept.) 1929.

attributed to a diet containing an insufficient quantity of iron is the most familiar example. Keefer and Yang [1] recently discussed the rôle of the various vitamins in the production of anemia and concluded that deficiencies of vitamin sufficient to cause keratomalacia, beriberi, scurvy, rickets, osteomalacia and tetany do not produce anemia and that if anemia is present in these patients it must be due to a deficiency of other substances or to some complicating factor, such as infection. With the patients of this series a hemoglobin value of less than 70 per cent was observed four times, but in other instances the blood picture was essentially normal. With so many existing complicating factors, no conclusion concerning the etiology of the anemia in these cases can be drawn.

Nutrition.—The general nutrition of practically all of the children of this series was far below the normal. In the absence of standard growth charts for Chinese children during the first few years of life and with the knowledge that the stated ages of many patients are often inexact, it is not possible to give accurate figures concerning the degree of undernutrition. The data given in table 2 were obtained by comparing the actual weights of the children with the average weights at different ages of normal American children as given by Holt and Howland.[27] Although the inaccuracy of this comparison is apparent, it is sufficient for the purposes of this paper, the deviations from the normal being so large as to be apparent by any reasonable method of comparison. The average weight of all the patients whose weights were known was 37 per cent below the normal. No conclusion is to be drawn from these figures except the inference that the food supply of these children was not only qualitatively but also quantitatively insufficient.

SUMMARY

1. Attention is called to the type of diet eaten by the average Chinese, to the high incidence in China of deficiency diseases in general and to the possibility of several deficiency diseases coexisting in the same patient.

2. A study of thirteen children with keratomalacia is presented, in which particular pains were taken to establish the presence or absence of other deficiency diseases.

3. It is shown that in some instances keratomalacia is associated with rickets, while in others it is not; also that previously active rickets may be healing at a time when keratomalacia becomes active. Reasons are given for the belief that the lack of association of rickets and kerato-

27. Holt, L. E., and Howland, J.: The Diseases of Infancy and Childhood, ed. 9, New York, D. Appleton & Company, 1926.

malacia in some patients is due to exposure to sunlight rather than to dietary factors.

4. No definite association of keratomalacia with beriberi was observed. However, the history of one infant is presented who exhibited moderate cardiac hypertrophy in association with rickets and keratomalacia. The size of the heart decreased following the addition of yeast to the diet.

5. No definite association of keratomalacia with scurvy was observed, although two patients presented purpura of obscure etiology.

6. The relation of edema disease to deficiency diseases in general is discussed. Five of the thirteen patients with keratomalacia showed edema. Reasons are given for the belief that in most instances this edema was a manifestation of some dietary fault distinct from that which caused the keratomalacia. The relation between diarrhea and edema in these patients is discussed.

7. The presence of anemia in some of the patients is noted, but no conclusions are drawn concerning its etiology.

8. Attention is called to the marked undernutrition of this entire group of children. The inference is drawn that their diets were not only qualitatively but also quantitatively insufficient.

Dr. S. M. Ling made the serum phosphorus and calcium determinations, Dr. C. K. Hsieh furnished the roentgenograms and Dr. A. Pillat confirmed the diagnoses of keratomalacia and granted permission to study several patients who were admitted on the ophthalmologic service.

HYPOPLASIA OF THE MANDIBLE (MICROGNATHY)

AS A CAUSE OF CYANOTIC ATTACKS IN THE NEWLY BORN INFANT: REPORT OF FOUR CASES *

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AND
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Atelectasis, congenital heart disease, intracranial hemorrhage and several other diseases are now recognized as producing cyanotic attacks in newly born infants, but little attention has been given to hypoplasia of the mandible as an etiologic entity in producing such attacks. During the past two years, four patients have been admitted to our wards on account of this condition.

REPORT OF CASES

CASE 1.—E. K., a white female infant, aged 6 weeks, was admitted to the hospital on account of failure to gain weight and frequent attacks of cyanosis. The family history was unimportant. The child was born at full term, with a normal delivery, weighing 8¼ pounds (3.7 Kg.). She was never breast fed but was given a formula on which she did not gain, though the formula was adequate. Soon after birth it was noticed that the infant had frequent and severe attacks of cyanosis, which could be relieved by placing her on her face, and exaggerated by placing her on her back. Similar attacks were produced when she was fed, and frequently she would vomit either all or part of the feeding. As the general course of the infant was not favorable, she was sent to the hospital. Physical examination showed a poorly nourished but fairly well developed white female infant with severe cyanosis and marked inspiratory embarrassment, as demonstrated by the supraclavicular and infraclavicular retractions and employment of all of the accessory muscles of respiration. The mandible was obviously shorter than normal and the tongue displaced posteriorly so that it rested against the pharyngeal wall and thereby occluded the respiratory passages. Cleft palate and a poor nutritional condition constituted the other observations. As the cause of the attacks was purely mechanical and could readily be relieved by placing the infant on its face and elevating the foot of the bassinet, no other procedures were necessary. However, as this was only a palliative form of treatment, other measures were considered. A small, light and efficient brace was made which is illustrated in the accompanying illustrations. Following the application of this support the attacks ceased, the baby nursed better, and when discharged from the hospital had gained 1 pound (453.6 Gm.).

CASE 2.—B. H., a white female infant, aged 3 days, was admitted on account of "blue attacks" and "tongue-swallowing." The family history was unimportant. The infant was born at full term by difficult forceps delivery, with laceration of

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the face and scalp and paralysis of the left arm. A few hours after delivery, the infant began to have cyanotic attacks which were worse when it was on its back and which were relieved by placing it on its face. A fatal prognosis was given on account of these attacks. On admission, the important observations were: a short and inefficient mandible, a tongue displaced posteriorly and obstructing the pharynx, a cleft palate, laceration of the scalp and cheek, left brachial paralysis, cyanosis and inspiratory embarrassment. A brace like that described for the first case was applied, and there was immediate relief from the symptoms.

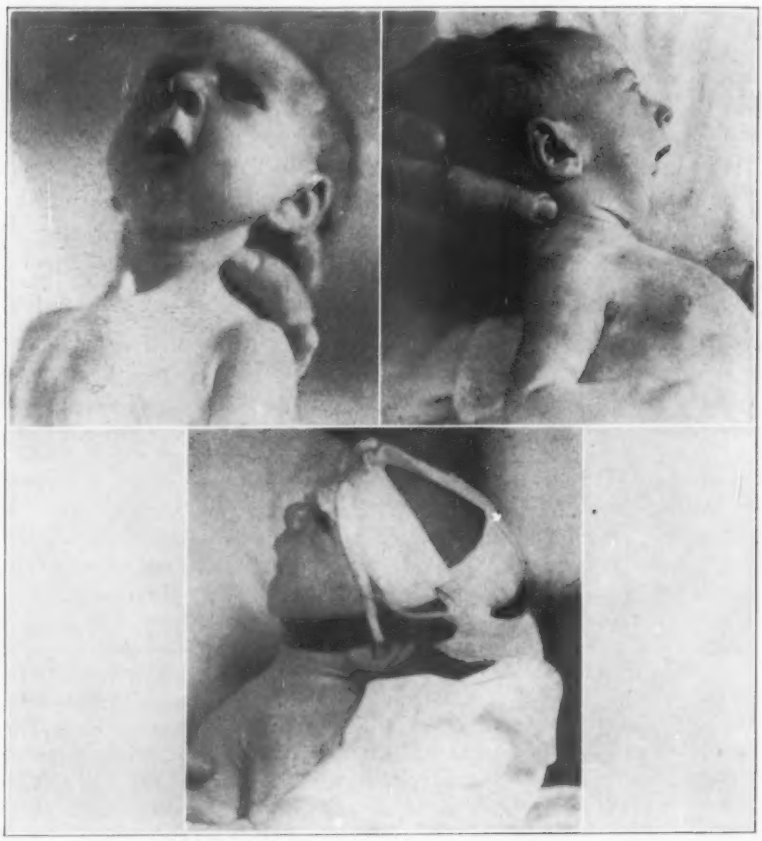

Fig. 1.—Case 1 (E. K.): typical facies and use of frame.

The patient gained in weight and was discharged from the hospital improved. She has been seen on subsequent visits to the outpatient department and is doing well.

CASE 3.—F. M., a white male infant, aged 10 days, was admitted to the hospital on account of recurrent attacks of cyanosis, regurgitation of food and failure to gain in weight. The family history was irrelevant. The infant was born at full term, with low forceps delivery, weighing 7¼ pounds (3.3 Kg.). Examination at this time apparently showed no abnormalities other than a cleft palate. During the first few days of life the mother noticed that the infant had frequent "blue

attacks," and that they were worse when it nursed or was placed on its back. The attacks became so frequent that the infant was sent to the hospital. Physical examination showed hypoplasia of the mandible, with the tongue displaced abnormally as described in the previous cases, cyanosis which was exaggerated when the infant was placed on its back or when it nursed, cleft palate and poor nutritional condition. As the hypoplasia was not marked, postural treatment was sufficient to prevent the attacks of cyanosis. When seen two years later the mandible had attained the normal size, the tongue no longer occluded the pharynx and the patient was in excellent nutritional condition.

Fig. 2.—Case 2 (B. H.): facies and use of improved frame.

CASE 4.—*History.*—C., a white female infant, was admitted to the hospital on the third day of life on account of recurrent attacks of cyanosis. The family history was unimportant. The patient was born at full term, with a normal delivery, weighing 5½ pounds (2.5 Kg.). The immediate postnatal condition was good. Soon after birth the infant began to have severe cyanotic attacks which increased in both severity and frequency until the time of admission. The physical examination showed marked inspiratory embarrassment, cyanosis, employment of all of the accessory muscles of respiration, hypoplasia of the mandible, posterior displacement of the tongue, causing obstruction of the pharynx and cleft palate. Two hours after admission an emergency tracheotomy was performed which gave

little relief. During the following eight days the condition of the patient became worse, and on the ninth day respirations ceased.

Autopsy.—Autopsy was performed twenty-eight hours post mortem. Examination of the brain was not permitted. The body was that of a well developed but poorly nourished white infant, 47 cm. in length. With the exception of the observations in the region of the head the main diagnoses were: (1) bronchopneumonia, (2) congestion of the lungs, spleen, liver and kidneys, (3) cloudy swelling of the liver, kidneys and suprarenals, (4) fatty infiltration of the liver, (5) thrush (*Oidium albicans*) of the oesophagus and (6) tracheotomy opening with ulceration.

The lower jaw was retracted in position in relation to the upper jaw. This retraction measured 8 mm. The lower lip was straight across and fissured at

Fig. 3.—Case 4 (B. C.): posterior view of gross specimen, showing the relation of the tongue (1) to the epiglottis (2).

the corners, and the upper lip was curved. The mouth was slightly open. The lower jaw could be moved forward for a distance of 1 cm. The temporomandibular joint showed no ankylosis. The alveolar ridges were well formed. The tongue lay quite far posteriorly and when pulled forward did not extend beyond the alveolar borders. The posterior half of the hard palate was completely absent, the soft palate being represented on either side by narrow bands of tissue. The nasal passages opened into the nasopharynx. The organs of the neck were removed with the mandible, which was disarticulated at the temporomandibular joint. It was then seen that the tongue lay back against the pharynx and above the epiglottis, causing obstruction of these two structures. The epiglottis was small but was well formed. The larynx showed no abnormalities. A tracheotomy opening was found at the midpoint of the thyroid gland, opening into the anterior surface of the trachea. Around the edges of the tracheotomy opening on the mucosal surface of the trachea there was a small amount of inflammatory reaction.

No marked necrosis or suppuration was present. The upper alveolar process, with the turbinates and the septal bone, was removed in one piece. The upper alveolar process measured 25 mm. anteroposteriorly and 35 mm. in width. The nasal pharyngeal opening through the cleft palate measured 20 by 15 mm. The nasal septum was deviated to the right, causing a partial obstruction of the right nares. The left nares appeared normal. The alveolar processes of the upper jaw were well formed. There was good union in the midline anteriorly, and the anterior portion of the hard palate was also well formed. The defect in the hard palate was convex anteriorly, forming a U-shaped opening with the

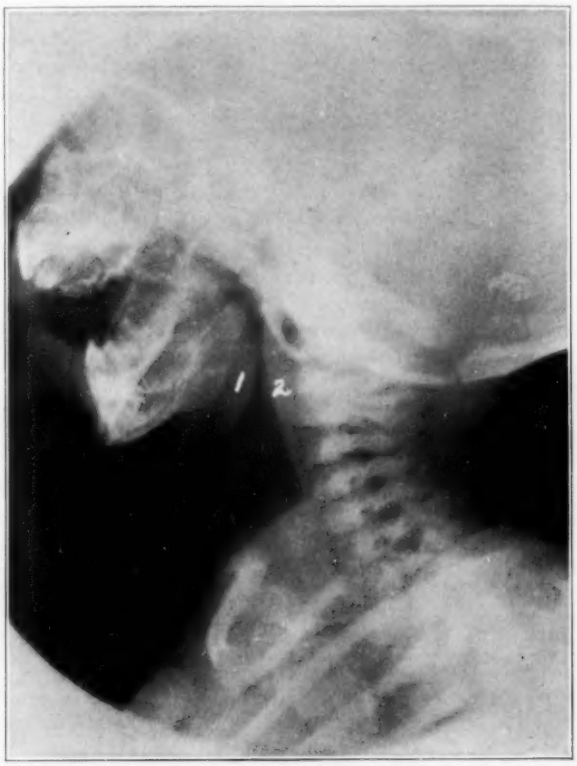

Fig. 4.—Roentgenogram showing the posterior displacement of the tongue (1) in case 4, with apposition to the pharyngeal wall (2) and the epiglottis.

opened end of the U directed toward the pharynx. Small bands of tissue passed from the right and left posterior pharyngeal wall to attach themselves to those parts of the hard palate which projected posteriorly as the lateral processes.

The mandible measured 40 mm. at its greatest width, taken midway between the symphysis mentis and the temporomandibular joint. Anteroposteriorly from the front of the temporomandibular joint to the plane of the symphysis mentis, it measured 35 mm. The anterior surface of the symphysis mentis and the anterior edge of the lower alveolar processes were nearly in the same vertical plane. The two rami of the mandible were well united anteriorly. The right ascending ramus of the mandible measured 22 mm. from the angle to the tip of the coronoid

process, and 20 mm. from the angle to the condyle. The mandible measured 35 mm. from the angle to the frontal plane at the symphysis. The distance between the angles of the right and the left rami was 50 mm. The lower alveolar process measured 34 mm. in width and 20 mm. anteroposteriorly. Comparing this with the alveolar process of the upper jaw it was seen that the lower alveolar process was 5 mm. shorter and 1 mm. less in width. These measurements linked up with the retracted appearance of the lower jaw before removal of the parts. No defects, points of separation or abnormalities were noted in the alveolar ridge of the lower jaw, with the exception of the measurements.

The anterior tip of the tongue was situated 6 mm. posterior to the anterior alveolar process of the lower jaw. The posterior portion of the tongue lay against the pharyngeal wall and rested on the epiglottis. The tongue lay at an angle of 90 degrees, bent on itself, measuring 20 mm. vertically and 25 mm. horizontally. The vertical portion of the tongue over its whole width and for a height of 20 mm. lay in direct apposition to the posterior pharyngeal wall. The tongue was thicker, shorter and broader than normal, lying well back in the pharyngeal space instead of forward in a horizontal plane. These observations explained the difficulty in respiration and feeding.

The esophagus was opened along its entire length, and the mucosal surface showed many areas of soft white cheeselike material, most abundant in the lower third of the esophagus, where the areas coalesced to form a homogenous exudate. This material could be scraped away with ease, and on microscopic examination showed the typical spores and mycelia of *Oidium albicans.*

The main diagnosis was: congenital anomalies of the mandible, tongue, palate and nasal passages: (1) hypoplasia of the mandible, with retraction of the tongue and obstruction of the pharynx and the epiglottis; (2) cleft palate, and (3) deviation of the nasal septum to the right, with obstruction of the right nasal passage.

COMMENT

Lenstrup [1] reported three of his own cases and collected two others from the literature, all of which presented symptoms similar to those observed in our cases; i. e., recurrent cyanotic attacks which were exaggerated by nursing or by placing the infant on its back and which were relieved by placing it on its face, and frequent vomiting and failure to gain in weight although the patient was receiving a formula adequate both in caloric content and in vitamins. Other interesting features were: The facies of these patients was striking, as the short mandible gave them a birdlike appearance; had cleft palates; roentgenograms showed a shadow in the pharynx and over the epiglottis which was due to the unusual position of the tongue, and all of the patients responded immediately to treatment.

Keibel [2] stated that in the first half of the third month of fetal life the two lips project about equally, but that later the border of the

1. Lenstrup: Hypoplasia Mandibulae as Cause of Choking Fits in Infants, Acta Pædiat. **5**:154, 1925.

2. Keibel and Mall: Manual of Human Embryology, Philadelphia, J. P. Lippincott Company, 1910, vol. 1, p. 86.

upper lip grows more rapidly, so that in the fourth and fifth month it projects markedly beyond the lower lip. By a greater growth of the lower jaw and lip this difference is gradually overcome. However, from the sixth to the ninth month of pregnancy, some inhibitory process may occur, and early fetal arrangement may be retained in the adult to a marked degree. According to Mall,[3] the mandible has reached its characteristic shape by the middle of the third month of fetal life. Feldman [4] described the mandible as incompletely developed at birth, with the ramus very small and not reaching complete development until the age of 3 years. The angle between the ramus and the body of the bone at birth is obtuse instead of almost 90 degrees as in the adult, and the mental foramen, instead of being midway between the lower and the upper margin, is nearer to the top, because the alveolar margin is not developed. As the child grows older the jaw is called on to accommodate the milk teeth and later the permanent teeth, at the same time, it has to withstand the more vigorous action of the hitherto weak muscles of mastication. As a result, the bone becomes stronger and alters its shape.

The characteristic features of this anomaly is the diminutive size of the lower jaw, with a retreating chin of an exaggerated type, producing a condition which is the opposite of cranium progenium in which the chin projects. Friesen [5] described the face of a micrognath as birdlike in profile. According to Perthes,[6] the horizontal portion of the lower jaw is affected more by the hypoplasia than is the ascending branch. The angle between the mandibular body and the ascending branch is decreased, the angle appearing in the form of a straight line directed downward.

From the ontogenetic point of view this anomaly of the jaw, like other anomalies of the lower jaw and ear, is associated with the first branchial arch and cleft and is due to imperfect development or irregular rearrangement of the tissues composing these transitory structures. Most authors agree that the anomaly is a simple arrest of development of the jaw. Keibel's explanation seems reasonable, especially in view of the later course in the development of the jaw under treatment. Pfaff [7] showed deformities to be hereditary in fifty cases and in some cases traced the deformity to several generations.

3. Keibel and Mall (footnote 2, p. 440).

4. Feldman: The Principles of Antenatal and Postnatal Child Physiology, New York, Longmans, Green & Company, 1920.

5. Friesen, quoted by Schwalbe: Die Morphologie der Missbildungen, Jena, Gustav Fischer, 1909, vol. 3, p. 550.

6. Perthes, quoted by Schwalbe, p. 551.

7. Pfaff, quoted by Bruening and Schwalbe: Handbuch der Pathologie des Kindesalters, Munich, J. F. Bergmann, 1913, vol. 2, p. 442.

In 1822 Saint-Hilaire [8] saw a case of hypoplasia of the lower jaw in a sheep, with conjunction of the ears, deformity of the palate bone and fusion of the pterygoid processes of the sphenoid. Because of the curious deformity of the sphenoid, Saint-Hilaire called the anomaly sphenocephalus and, as Ballantyne [9] expressed it, therefore initiated a series of terminological and classificational difficulties. Since this anomaly has been found in combination with many other anomalies associated with the first branchial cleft and arch, there have been many complicated names suggested. In 1891 Taruffi [10] tried to bring some order into this chaos of confused classifications and nomenclature; he made one group to include all the malformations showing defective development of the lower part of the face and called it hypoprosopo-aplasia. He subdivided this into hypomicrognatus (small lower jaw) and hypoagnathus (absence of the lower jaw). The deformity may be bilateral or unilateral, and it may be of medium or high degree. When of high degree, it is usually associated with actual defects in the jaw. It is not infrequently accompanied by unilateral or bilateral ankylosis of the temporomandibular joints. Perthes described one case noted soon after birth in which the joints were ankylosed. The patient grew to adult life and showed the typical face of the micrognath. In 1891, Lannelongue and Ménard [11] described a series of cases of bilateral micrognathus. In one of these, a girl, aged 2 years, the upper part of the face was normal in appearance, while the lower lip lay in a plane posterior to the upper lip and the lower jaw failed to make the usual projection; the cheek passed directly into the neck, while the mandible not only was displaced posteriorly but was atrophic. Anteroposteriorly there was a distance of about half an inch between the teeth of the upper and those of the lower jaw, accompanied by bilateral ankylosis of the temporomandibular joints. The clinical result of the malformation was difficulty in feeding. In the other two similar cases reported by these authors the difficulty was intensified by the coexistence of cleft palate, resulting in the death of one of the patients at the age of 23 days. The tongue was small and was accommodated in the nasal fossae. In another case there were other anomalies associated with the condition of the jaw, including congenital club foot, scoliosis and muscular weakness.

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8. Saint-Hilaire: Philos. Anat., 1822, vol. 2, p. 97, quoted by Ballantyne (footnote 9).

9. Ballantyne: Antenatal Pathology and Hygiene, New York, William Wood & Company, 1905, vol. 2, p. 423.

10. Taruffi: Storia della teratologia, Bologna, 1891, vol. 6, p. 389.

11. Lannelongue and Ménard: Affections congénitales, Paris, Hasselin & Houzeau, 1891, vol. 1, p. 423.

Ballantyne, who cited a case reported in 1860 by Hampton, stated that at times micrognathy may be unilateral. Other cases were collected and reported by Taruffi [12] in 1891, Maurice [13] in 1861, Marc [13] in 1892, Buerger [13] in 1903, and by many other authors. Virchow [14] in 1864 described two cases that were associated with malformations of various types. Perhaps the most constantly associated condition is cleft palate, and, as Lenstrup stated, "it is certainly most probable that the cleft palate is a consequence of the same developmental inhibition that produces hypoplasia of the lower jaw, and that its presence is a coordinate phenomenon without any independent significance." In the human being complete absence of the lower jaw is comparatively rare, although a few cases have been reported. The condition is much more common in the lamb, possibly due, as Ballantyne suggests, to some undiscovered peculiarity in the ontogenesis of that animal.

CONCLUSIONS

Obviously, the treatment for this condition is directed toward those measures that will prevent the tongue from being displaced posteriorly. In cases in which the hypoplasia is not marked, postural measures alone are sufficient, for by placing the infant on its face and elevating the body the tongue will remain in its normal position by virtue of its own weight. In the more severe cases, in which posture alone is not sufficient, the brace, as illustrated in the accompanying illustrations, will be as satisfactory as it is simple. This consists of a strong piece of copper wire which rests on a soft flannel band as it passes across the forehead and which is shoed with rubber tubing as it passes down the side of the face to the angle of the jaw. Here it passes under the ramus, forming a right angle to the descending limb. The two ends of the frame are then joined by a piece of white tape which holds the frame firmly in position and tends to maintain the pressure that is exerted against the mandible and the floor of the mouth. The mandible is then displaced forward, and at the same time pressure is exerted against the floor of the mouth and the base of the tongue. Surgical procedures, such as suturing the tip of the tongue to the lip and tracheotomy, may be used, but in our experience such measures were not necessary. Efficient nursing plays an important rôle, as these patients are difficult to feed not only on account of the short mandible but also on account of the cleft palate.

12. Taruffi (footnote 10, p. 391).
13. Quoted by Ballantyne (footnote 9, p. 427).
14. Virchow: Arch. f. path. Anat. **30**:221, 1864.

THE RESPONSE TO PLANTAR STIMULATION IN INFANCY *

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In every piece of experimental work two steps seem to be necessary. The first is the development of an appropriate method for studying the problem; the second is the actual study.

The variability of technic reported in the literature often makes it difficult to determine for any given problem the method which takes into full consideration the present accumulation of facts and theories. This seems to be particularly true for the study of reflexes. The flood of papers describing single reflex responses has reached a point at which it is difficult to keep track of fundamental principles.

In this paper, I attempt to attack the study of plantar stimulation in infancy in the two ways described. The first part deals with the analysis of the observations contained in the English, French and German literature for the purpose of setting up a method of studying the response to plantar stimulation. The second part deals with the application of such a method to my material.

REVIEW OF THE LITERATURE

The literature includes the description of response to plantar stimulation in supposedly normal persons, the interpretation of the response to such stimulation in connection with diseases and malformations of the nervous system, a vast array of observations from experimentation on animals, and relatively few contributions on the developmental aspect of response to this particular stimulus. At present, however, the last named phase is receiving increasing attention.

Long before Babinski described the distinctive reaction of the big toe in lesions of the pyramidal tracts, Kussmaul,[1] Preyer,[2] Genzmer [3] and others had noted in young infants toe and leg responses to tickling and stroking of the sole. Since the publication of Babinski's [4] first

* Submitted for publication, Nov. 11, 1929.

1. Kussmaul, A.: Untersuchungen über das Seelenleben des neugeborenen Menschen, Leipzig and Heidelberg, F. Pietzcken, 1859.

2. Preyer: Spezielle Physiologie des Embryo, Leipzig, 1885; Die Seele des Kindes, 1895; Die geistige Entwicklung in der ersten Kindheit, T. Grieben, 1893.

3. Genzmer, A.: Untersuchungen über die Sinneswahrnehmungen des neugeborenen Kindes, Halle, Ploetz, 1873.

4. Babinski: Du phenomeme des orteils et de sa valeur semiologique, Semaine méd. **18**:321, 1898.

paper in 1898, a large number of studies have dealt with case histories and the occurrence of the Babinski phenomenon in connection with various groups of nervous disorders. I shall pass by these investigations without much comment, as this study is concerned with the developmental rather than the clinical aspect of the phenomenon.

Babinski himself did but little work on infants, and although such early observers as Cohn [5] Schüler [6] and Morse Lovett [7] made some investigation of the Babinski reflex in early childhood, it remained for Engstler [8] to publish in 1905 the first study in which the subjects were segregated into age groups at sufficiently small intervals to bring out developmental differences. Following these observations, there are a number of studies based on varying material and widely varying technic. Thus a few investigators, of whom Minkowski [9] has made the most important contribution, have experimented with a number of fetuses obtained by cesarean section under local anesthesia. Others have occasionally tested a few children together with a small number of adults, while in a few instances as many as 1,000 children of various age groups have been examined and the results utilized for the study of development in nervous integration.

The methods used to elicit the plantar response and the descriptions of resulting movements vary greatly among the different authors. Only a few observers give any accurate description of their technic, but these few demonstrate sufficiently the discrepancy of methods. Nine years after the publication of his first paper, Babinski [10] himself stated that the phenomenon changes according to the part of the sole to which the stimulus is applied, and that, for example, stroking of the outer border is more apt to elicit the phenomenon than stroking of the inner border of the sole. Cohn,[5] in 1899, emphasized the point that the leg of the subject should be held firmly while the stimulus is

5. Cohn, M.: Ueber die Bedeutung der Zehenreflexe, Neurol. Centralbl. **18**:580, 1899.

6. Schüler, L.: Beobachtungen über Zehenreflexe, Neurol. Centralbl. **18**:585, 1899.

7. Lovett, Morse John: A Study of the Plantar Reflex in Infancy, Neurol. Centralbl. **20**:449, 1901.

8. Engstler: Ueber den Fussohlenreflex und das Babinskische Phänomen bei 1,000 Kindern der ersten Lebensjahre, Wien. klin. Wchnschr. **18**:567, 1905.

9. Minkowski, M.: Zum gegenwärtigen Stand der Lehre von den Reflexen in entwicklungsgeschichtlicher und anatomisch-physiologischer Beziehung, Schweiz. Arch. f. Neurol. u. Psychiat. **15**:239, 1925; **16**:133 and 266, 1925; Ueber frühzeitige Bewegungen, Reflexe und muskuläre Reaktionen beim menschlichen foetus und ihre Beziehungen zum foetalen Nerven und Muskelsystem, Schweiz. med. Wchnschr. **3**:721 and 771, 1922; Zur Entwicklungsgeschichte, Lokalisation und Klinik des Fuss-sohlenreflexes, Schweiz. Arch. f. Neurol. u. Psychiat. **13**:474, 1923.

10. Babinski, quoted by Kalischer, Otto (footnote 11).

applied, since the movements of the foot tend to mask the movements of the toes. Kalischer [11] put the legs of his patients across his knees and scratched the sole in the longitudinal direction. Later observers stressed the importance of the smoothness of the testing instrument. Kalischer also emphasized the influence of cold feet, which tends to diminish the response, an observation restated in 1910 by Fleischner,[12] who, of all the early observers, has given the most complete description of technic. He suggested, as did Engstler in 1905, that the reaction following the first stroke should be the one recorded, and that the results are comparable only when the children are quiet and when the greatest caution is taken to remove shoes and stockings without disturbance. He believed that exact standardization of the stimulus is impossible, but that the lightest stroke capable of eliciting response should be used. Later authors, especially the French, gave similar instructions. Thus, Rosenblum [13] (1915), describing her method, mentioned that all infants with whom she worked were lying on their backs and that their attention was distracted during the testing of the plantar response. The last factor seems to be important, as Babinski stated that the responses increase when the subject is not distracted.

Just what should be noted after the plantar stimulus has been applied is another point concerning which the literature shows wide variation of opinion. A great number of authors limit their observation to the movements of the toes and their differentiation. They report that other movements result, but consider only the movements of the toes significant. Bersot [14] took an altogether different attitude. He claimed that not only the form of response, but also the number of muscle groups taking part in the reaction is important; he found that the number of responding muscle groups decreases, and that the reactions concentrate during the first decade into a mature form which remains constant for about two decades and then dissolve again into a number of reactions in senility. The objection that some of the resulting movements may be voluntary he meets with the argument that he has observed this summation of reactions in narcosis and during sleep; further, that the distinction between voluntary and involuntary movements is some-

11. Kalischer, Otto: Ueber den normalen und pathologischen zehenreflex, Virchows Arch. f. path. Anat. **155**:486, 1899.

12. Fleischner, Charles: The Plantar Reflex in Infancy and Childhood, Arch. Pediat. **27**:586, 1910.

13. Rosenblum: Du développement du système nerveux au cours de la première enfance, Thèse de Paris, 1915.

14. Bersot, H.: À propos du reflexe plantaire, Arch. internat. de neurol., 1923 and 1924, vols. 16 and 17; Developpement reactionelle et reflexe plantaire du bébé né avant terme a celui de deux ans, Schweiz. Arch. f. d. Neurol. u. Psychiat. **7**: 212, 1920; 1921, vol. 8.

what arbitrary in any case and depends on the interpretation of the observer. In recording everything that happens after one stimulus has been applied, Bersot revived some of the old methods, used primarily in diary records, but applied to more extensive material, carefully analyzed and submitted to statistical treatment. He noted that the normal trend of development is interrupted by disease as well as by fatigue; during these stages, infantile forms of response to the plantar stimulus may appear more frequently.

As might be expected, the wide range in technic and the difference in interpretation pervade the clinical field of investigation on the plantar response as extensively as they do in the physiologic field. The majority of observers approaching the problem from the clinical side, however, have emphasized the significance of the movements of the big toe alone, and only in relation to various nervous disorders. They have agreed that hyperextension of the big toe is pathognomonic for the direct or indirect interference with the conduction of nerve impulses along the pyramidal tracts. A few investigators have attempted to evaluate not only the movements of the big toe as response to plantar stimulation, but the whole complexity of resulting muscular phenomena in toes, foot and leg.

Thus Bing [15] differentiated the abnormal plantar responses into four types: (1) pure Babinski; (2) extension of all toes; (3) simultaneous twitchings in the tensor fasciae latae, adductores or quadriceps femoris; (4) retraction of the whole leg, which is commonly called flight reaction. In cerebral lesions, Bing found the pure Babinski predominant, while in two thirds of the spinal lesions he observed the other types.

Among the observers who have worked on the developmental aspect of the problem, there is general agreement that the Babinski phenomenon does not represent a pathologic symptom in infancy. Some authors deny its occurrence, while those who find it present differ as to the age at which the Babinski phenomenon gains pathologic significance. Some insist that its occurrence after the first year is abnormal; others consider it a normal phenomenon up to 3 years. No particular importance has been attributed to the time when the mature form of the plantar response becomes established. It has been observed, however, that rachitic children develop the plantar response later than healthy children, but in any case before they learn to walk. On the other hand, cases have been observed in which the Babinski response persisted after the walking function had been acquired. No correlations between the development of the plantar reflex, the form of walk-

15. Bing, R.: Varietaten des Babinskischen Reflexes, Schweiz. Arch. f. Neurol. u. Psychiat. **3**:89, 1918. Ueber Varietäten des Babinskichen Zehenreflexes und ihre diagnostische Bedeutung, Cor.Bl. f. schweig Aerzte, 1915, no. 39.

ing and the functional development of the foot have been made. Although it is generally assumed that the form of the plantar response depends on the development of the nervous system, the whole problem of correlating the development of plantar response to other neurologic phenomena has been touched only superficially.

The identification of the several forms of plantar response occurring in nervous disorders of adults with the infantile stages of the phenomenon has been frequently suggested, and such an hypothesis seems inviting; however, to me it does not seem logical to identify an organismal response, in which one regulating factor has been destroyed, with a response in which the same regulating factor has not yet developed since this factor, once in existence, influences widely the whole network of the nervous system; this influence cannot be entirely destroyed, even if the original anatomic unit is injured.

In the attempt to explain the Babinski and similar phenomena during infancy, every part of the reflex arc has been offered as being responsible. It has been suggested that: (1) the peripheral nerve is not sufficiently myelinated at birth; (2) the fibers of the extensor muscles are further developed at birth than the fibers of the flexor muscles; (3) the tonus of the extensor muscles is higher at birth than that of the flexor muscles, and a stimulation from outside takes the path of least proprioceptive tonicity; (4) the pyramidal tracts are insufficiently myelinated at birth; (5) the brain cortex of the infant does not exert inhibitory control; (6) the phylogenetic change of the foot from a grasping organ into a supporting organ is repeated in the development of the person; (7) the Babinski in the infant is not identical with the Babinski phenomenon in organic lesions, but it falls in line with the athetotic movements of the new-born infant resulting from the influence of the corpus pallidum without the influence of the corpus striatum.

From the developmental point of view, the most interesting theory is that of Minkowski.[9] His experimental work on the fetus has led him to believe that the final appearance of the plantar response in the adult is the algebraic sum of different components representing various flexion and extension values, each of these mediated by a different part of the central nervous system. These components come into play successively during development. He expressed the belief that the reaction in the very young fetus is limited to the muscular system without intervening nerve conduction, while the development of the true reflex arc takes place during later stages of prenatal existence. He expressed the belief that at birth impulses from the midbrain are already effective, causing extension of the toes, while spinal centers alone would cause plantar gripping. The younger the baby, the fewer the factors that come into play, and therefore the final effect is more labile.

EXPERIMENTAL WORK

On the basis of the variety of observations described and following especially the work of Bersot, I have studied my material. This study of the plantar response is included in a variety of observations concerning growth and development of sixty normal infants. They were first seen in the hospital during the first week of life. After that they came, and still come, at monthly intervals to the Institute of Child Welfare in Berkeley where the same observers do their work in the same surroundings. The technic used in the study of the plantar response of these children follows in detail.

The stimulus is applied while the subject lies on his back, and while he is awake but quiet. Any variation from these conditions is recorded. The stimulus is applied lightly with the smooth handle of a reflex hammer. The legs and feet of the subject are touched as little as possible previous to and during the test, but care is taken that the feet are not cooler than the rest of the body surface. The stimulus is applied along the outer border of the sole and the reaction to the first stroke is noted; if more stimuli are applied the responses are recorded in their sequence. Every resulting movement is recorded.

At the time this article was prepared, most of the infants had gone through their examination at 5 months and more than half of them at 6 months.

The number of observations at each month was as follows:

Month	0	1	2	3	4	5	6	7
No. of infants	53	51	57	57	55	54	35	27

The number of observations at monthly levels never equals sixty, because the test was omitted when the standard situation could not be established. For this reason the number of observations varies each month, even if the full sample has reached the age considered.

In the tabulation for statistical treatment the toe responses to the plantar stimulus were classified as:

B True Babinski (isolated slow hyperextension of the big toe)

D Dorsal extension of all toes with or without fanning

P Plantar grip

O No toe reaction

M Mixed reaction (dorsal extension of toes followed immediately by plantar grip or vice versa without new stimulation)

AR Asymmetric reactions. *M* on one foot and *O* on the other occurring together or either one with *P* were not considered to be asymmetric, since they contain the plantar factor. In the mixed reaction this factor is already present; when no toe reaction occurs, the plantar factor is sufficiently developed to suppress extension

Figure 1 serves to illustrate three of the fundamental reactions to the plantar stimulus. The positions of the toes in these pictures did not occur after stimulation, but represent spontaneous positions.

The most frequent reaction during the first few months of life is not the typical Babinski but the dorsal extension of all toes. Few plantar grips occur, and they are not consistent from month to month. As time goes on, the percentage of the plantar grip (*P*) rises quickly, and the dorsal extension of the toes (*D*) loses importance. Mixed reaction (*M*) and no toe reactions (*O*) show irregular tendencies;

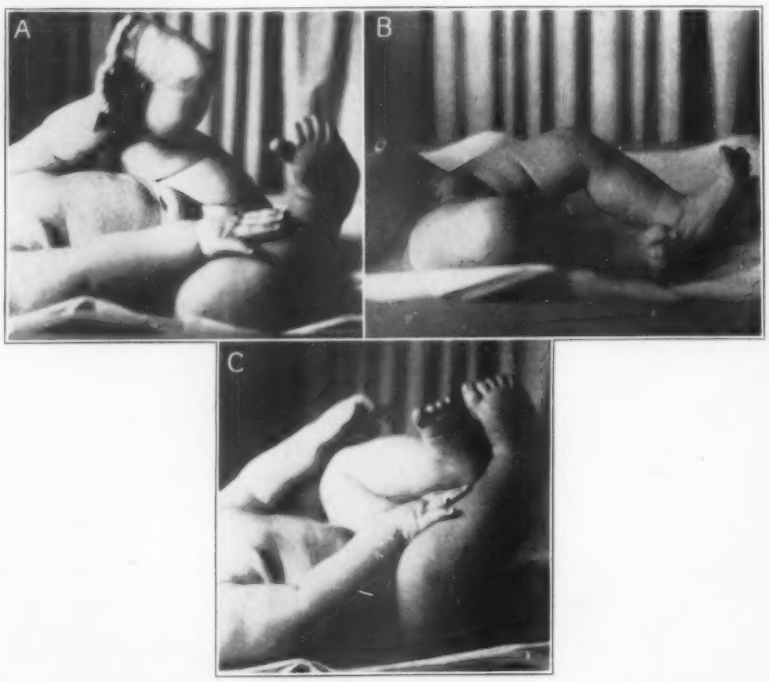

Fig. 1.—*A*, true Babinski reflex; *B*, dorsal extension of all the toes (left foot); *C*, plantar flexion.

they never remain consistent reactions and may be considered as intermediate stages preparing the way for the establishment of the plantar grip. The classic Babinski was observed only 13 times out of 389 observations, slightly more frequently during the earlier months of life but at all times the least frequent of all responses described.

My next consideration takes advantage of the special nature of my material. The plantar response (*P*) was considered to be "established" when it had been observed three times in succession without being followed by a contradictory response. For this determination, only those

infants who had at least passed through their fifth month examination were used. The increase in the percentage of cases which show the plantar response established does not rise steadily; the largest increase occurs between the second and third months. By the fifth month, for which I have observations on fifty-four cases, the number of infants showing an established plantar response totals twenty-two, or 42.9 per cent. It is obvious that no direct relation to the development of the walking function exists at this age. The time of the first appearance

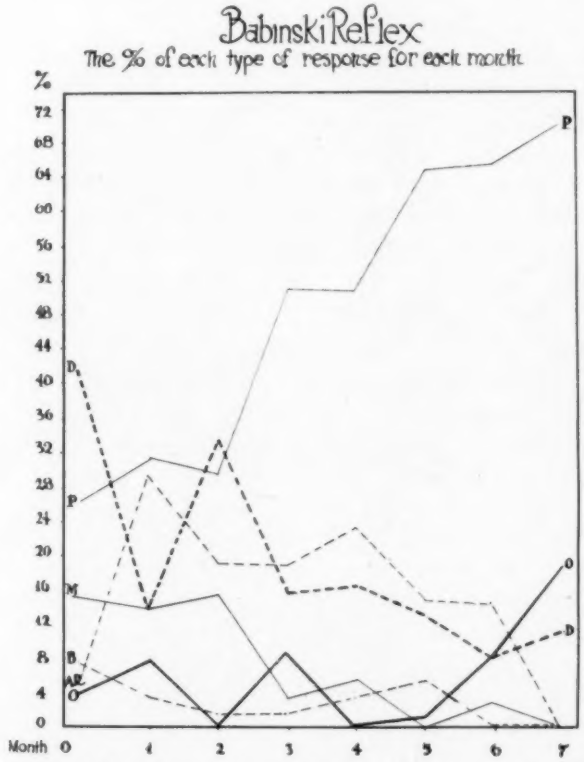

Fig. 2.—Babinski reflex; the percentage of each type of response for each month. *P*, plantar response; *B*, Babinski reflex; *D*, dorsal extension of toes; *M*, mixed reaction; *O*, no toe response; *AR*, asymmetrical response.

of the plantar grip is not indicative of an early establishment of this response. Many erratic plantar responses occur during the early months of life, indicating only the great lability of the infantile nervous system so far as reflex action is concerned. This clearly demonstrates the importance of cumulative studies on the same child, since an isolated response may be erroneously considered as typical if the child is seen only once.

The number of asymmetric responses has practically nothing to do with the time the plantar grip becomes established. This is contrary to what might be expected, but it must be admitted that outside factors play an important part in the appearance of asymmetric reactions. Slight differences in the original position of the feet and toes and circulatory differences may be responsible for these phenomena; it does not seem likely that they are based on anatomic asymmetry, especially as no other evidence of asymmetric nerve function has been encountered in these cases.

I called those observations inconsistent which showed one type of response one month and another the following month; thus a record showing *BPDPP* is considered as showing three inconsistencies (*M*, *O* and *P* were not considered contradictory to each other for reasons previously mentioned). The percentage of inconsistent reactions for each case was secured by comparing the actual number of inconsistent reactions to the possible number of inconsistent reactions; the latter was indicated by the number of the final month of examination less 1. If inconsistency in the reaction type is an expression of infantile lability, as has been stated by others, this inconsistency should correlate markedly with other indexes of immaturity. As the earlier evidence indicates, *B* and *D* represent such factors. Hence, on the hypothesis that inconsistency is a mark of immaturity, the higher percentages of inconsistent reactions should occur in those cases which show the greatest persistence of *B* or *D*. This is actually the case, as is shown by a correlation of 0.77 ($\pm$ 0.05) between the percentage of inconsistent reactions and the persistence of *B* or *D*.[16]

Considering the question to what extent the reaction to plantar stimulation involves separate muscle groups, no tendency toward increase or decrease could be detected with increasing age during the first seven months of life. The number of separate muscle groups reacting varies greatly; simple toe response on the one hand and the complex flight reaction on the other represent the extremes; however, all intermediate combinations of movements are represented at each month level considered. The variability in the number of movements is much greater in each case than the variability in the type of toe movements. This fact may be explained by the great number of proprioceptive impulses which flow from the large joints of the leg to the spinal cord. Only an unusual coincidence could bring about that all joints of both legs would be in exactly the same position at one examination or that this position would be the same during successive tests. It follows that

16. As expressed by the ratio: $\frac{\text{Last month in which B or D appears}}{\text{Last month of observation to date}}$

the successful study of the decrease in responses by separate muscle groups must await later stages of development of inhibitory control by the higher centers. So far as the responses to plantar stimulation are concerned, there is evidence that this tendency has started at the seventh month.

SUMMARY

A review of the literature dealing with the Babinski phenomenon is presented. Special emphasis is placed on the observation in children.

Discrepancies in the technic of studying the phenomenon are pointed out.

The more commonly accepted theories concerning the neurologic basis for the Babinski phenomenon are enumerated.

A technic for the study of the responses to plantar stimulation is described.

The results of an investigation are given which deals with observations following plantar stimulation in sixty healthy infants tested at monthly intervals over a period of seven months.

CONCLUSIONS

From the literature already published, no satisfactory conclusions can be drawn concerning the appearance, disappearance or developmental significance of the several responses to plantar stimulation during infancy because of the wide variation in subjects and technic, and because of the lack of cumulative studies. The study of the plantar response requires a carefully standardized technic uniformly applied.

The classic Babinski phenomenon occurs but rarely during the first six months of life.

Dorsal extension of all toes with or without fanning is the most frequent response during the early months.

At the seventh month a high percentage of cases show consistently the characteristic flexion of all toes to plantar stimulation.

Variation of response as between the two feet is not an expression of anatomic asymmetry.

HUMAN MILK FLOW*

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AND

BETTY NIMS

DETROIT

Though many rational theories have been advanced on the subject, it is not known whether nervous, chemical or glandular agents operate to start the flow of milk. Even seemingly convincing experimental evidences are contradictory concerning the causes of the hypertrophy of the mammary glands during pregnancy and their secretory activity immediately after parturition. There is a general opinion that nervous shock, certain psychic states caused by the presence or absence of the suckling reflex and the emotional status and environment of the mother affect the flow of milk. The perturbation accompanying these factors is evidently not a direct nervous mechanism, since it has been shown experimentally that the severance of the spinal cord in woman [1] and in other mammals [2] and of the nerves supplying the mammary glands [3] causes no untoward influence on the secretory activity of the glands. This evidence is further substantiated by the results of an experiment in which two mammary glands of a guinea-pig were transplanted into the skin back of the ear of a sister animal.[4] A few months later, the experimental animal conceived and bore young, and the two mammae in their new environment were seen to function normally, i. e., they became

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† National Research Council Fellow in Child Development and Parent Training under a grant of the Spelman Fund, 1927-1928, and National Research Council Fellow in Child Development under a grant of the Spelman Fund, 1929-1930.

1. Routh, Amand: Parturition During Paraplegia, Tr. Obst. Soc., London (1896), 1897, vol. 35.

2. Goltz, F., and Ewald, J. R.: Der Hund mit verkürzten Rückenmark, Arch. f. d. ges. Physiol. **62**:362, 1896.

3. Eckhard, C.: Die Nerven der weiblichen Brustdrüse und ihr Einfluss auf die Milchsecretion, Beitr. z. Anat. u. Physiol., 1877, vol. 8.

4. Ribbert, Hugo: Ueber Transplantation von Ovarium, Hoden und Mamma, Arch. f. Entwcklngsmechnik. **7**:688, 1898.

hypertrophied during pregnancy, developed normal mammary tissue, and secreted milk in the lactation period. Thus, it would seem that any effect the nervous mechanism may have on the flow of milk operates indirectly through other glands or organs in the maternal body which are known to produce hormones influencing mammary activity.

The increased circulation of blood after the discharge of the fetus has been considered to be one factor in the initiation and continuation of milk flow, and the presence in the blood of particular chemical excitants which favor milk formation another. The evidence concerning the influence of chemical excitants in the blood is the more convincing, but it is impossible at present to say whether these hormones or galactagogues have their source in the placenta, in the fetus or in certain glands of internal secretion. In general, however, there seems to be an intimate relation between the expulsion of the fetus and the remaining uterine contents and the initiation of lactation, though anomalous instances of the secretion of milk by virgins,[5] males [6] and infants [7] are cited in the literature.

The present report deals with the hourly, daily and monthly fluctuations in the secretion of human milk during two successive lactation periods in each of three subjects, with notes on breast capacity and a method of stimulating quantity production. It is one of a series of reports on a study of the factors influencing the secretion of human milk after the establishment of milk flow. In this study the customary fluctuations in the volume output of each of the subjects throughout a continuous lactation period have been determined, and the volume output from the two breasts at rhythmic intervals during the day and night, from day to day and from month to month, in successive lactation periods, has been observed.

EXPERIMENTAL PROCEDURE

The following women, subjects of this investigation, lived normal lives within their own families and ate their customary diets during the entire study:

Subject 6, a quartipara, successfully supplied milk in excess of what her babies needed. The excess milk has been sold to the Mother's Milk Bureau

5. Hill, Ruben L.: An Exceptional Case of Milk Secretion and Its Bearing on the Theories Concerning Mammary Development, J. Dairy Sc. **2**:19, 1919. Marshall, Francis H. A.: The Physiology of Reproduction, ed. 2, London, Longmans, Green & Company, 1922, p. 617.

6. Deaver, John B., and McFarland, Joseph: The Breast: Its Anomalies, Its Disease, and Their Treatment, Philadelphia, P. Blakiston's Son & Company, 1917, p. 16. Knott, J.: Abnormal Lactation; in the Virgin; in the Old Woman; in the Male; in the Newborn of Either Sex, Am. Med., 1907, vol. 2.

7. Wieczorek: Fall von ausserordentlicher Schwellung und Sekretion der Brustdrüsen beim Neugeborenen, Deutsche med. Wchnschr. **49**:916, 1923.

of Detroit. During her first lactation period, she sold 14,140 ounces, which, with a brief period of wetnursing, yielded an income of $2,128; during her second lactation period, she sold 15,895 ounces of milk for $1,589. This woman was under our continuous observation during the third and fourth periods, designated in this report as lactations A and B, respectively. She has inverted nipples, and has therefore expressed all of her milk and fed her babies by bottle.

Subject 7, a tripara, was a successful milk producer. During the first lactation period she produced 20,196 ounces more milk than her baby took. This excess milk was sold to the Mother's Milk Bureau for $2,020. This subject was under continuous observation throughout the second and third periods, referred to in this study as lactations A and B, respectively. In lactation A, she nursed her baby and manually expressed the excess milk, except during special experimental periods, when the baby was removed from the breast; but in lactation B, she expressed all of her milk and fed her milk to the baby by bottle.

Subject 8, a duipara, though not as heavy a milk producer as her sister, subject 7, produced a considerable amount of milk beyond that which her baby took. During her first period, lactation A, she sold 4,486 ounces of milk at the Mother's Milk Bureau for $670. Throughout her second period, lactation B, she was under continuous observation and expressed all of her milk by hand and fed the baby by bottle.

Psychologic, physiologic, chemical and nutritional observations[8] accompanied this study of milk flow. The women recorded their own body weight and the weight of their babies at weekly intervals. The food intake of the women was weighed during the day of special milk study and during the preceding day. The kind and amount of liquids taken as beverages were recorded throughout lactation B by all three subjects. The milk was completely expressed regularly two or three times daily, except during special milk studies, when the breasts were emptied at four-hour intervals throughout the twenty-four-hour day, in periods of successive days, and at twenty-eight-day intervals during each of two successive lactation periods. All collections were made in the subject's home under the supervision of one of the writers (H. H.

8. Macy, I. G.; Hunscher, H. A.; Nims, B., and Schimmel-McCosh, S.: Metabolism of Women During the Reproductive Cycle: I. Calcium and Phosphorus Utilization in Pregnancy. Hunscher, H. A.: II. Calcium and Phosphorus Utilization in Two Successive Lactation Periods. Macy, I. G.; Hunscher, H. A.; Schimmel-McCosh, S., and Nims, B.: III. Calcium, Phosphorus, and Nitrogen Utilization in Lactation Before and After Supplementing the Usual Home Diets with Cod-Liver Oil and Yeast, J. Biol. Chem. **86**:19, 1930. Hunscher, H. A.; Vincent, E. L., and Macy, I. G.: Psychological Studies: I. The Technique of Securing Quantitative and Coordinated Psychological and Physiological Data on Lactating Women in Their Usual Home Environment, J. Child Development, 1930, vol. 1.

A series of papers on the chemistry of mother's milk secreted under varying conditions and the urine that is simultaneously excreted, accompanied by blood analyses and records of the quality and quantity of food consumed are to be published in the near future.

or E. D.), who lived there as a member of the family during the special milk, dietary, psychologic and metabolic studies.

This report deals, then, with data collected during two successive lactation periods of each of three women who were able to produce more milk than their babies needed. Subject 6, in two successive lactation periods, and subjects 7 and 8, in one period, manually expressed their total milk supply and kept a continuous daily account of their complete milk production. The total quantity of milk secreted, then, is recorded for four lactation periods, each of fourteen months' duration, and in the absence of the suckling reflex, in three different women, two of whom are sisters.

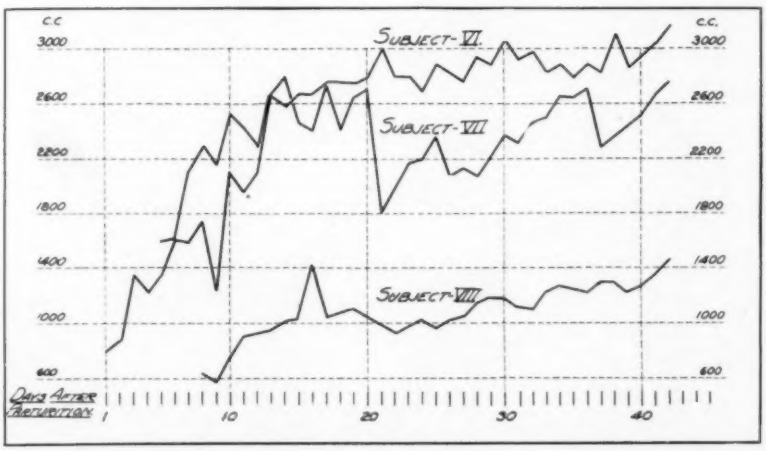

Fig. 1.—Daily variations and the gradual increases in total quantity of milk produced by three women in twenty-four-hour periods throughout the first six weeks of lactation. The entire milk supply was manually expressed two or three times daily.

EXPERIMENTAL DATA

There are marked variations in the quantity of milk secreted by the individual woman from day to day. Figure 1 shows the daily fluctuations that have been observed in three women, subjects 6, 7 and 8, during the first six weeks of a lactation period. Although there were distinct daily variations, there was a gradual increase in the quantity of milk produced as lactation progressed. These observations are in accord with those of Brodsky [9] and Laurentius,[10] who studied several

9. Brodsky, C.: Beobachtungen über die Lactation der Ammen, Arch. f. Kinderh. **63**:161, 1914.

10. Laurentius, Johannes: Zur Leistungsfähigkeit der Brustdrüse der Ammen, Arch. f. Kinderh. **56**:275, 1911.

wetnurses over varying intervals of the lactation period. The results of their observations are summarized in figure 2. The composite curve has been constructed by determining the mean increase in milk output from day to day in twenty-two women reported by them. This curve, together with those presented in this paper, though based on observations on large milk producers, do represent the increase in the impulse to secrete milk as early lactation progresses.

Just as there is a wide daily fluctuation in the amount of milk secreted by individual women, so there is a variance in the quantity output from week to week. The gradual increase in milk flow is evidently peculiar not only to the individual but also to each particular

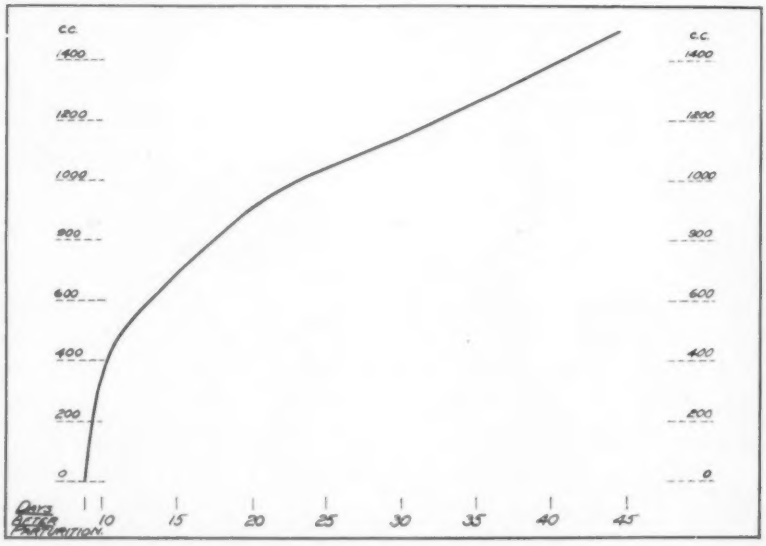

Fig. 2.—Curve showing the tendency toward a gradient in the production of breast milk during the first six weeks of lactation. This curve is based on the daily milk production records of twenty-two women. (Compiled from records of Brodsky and Laurentius.)

lactation period (figs. 3, 4, 5 and 6). The tendency toward increased flow may progress up to the sixth week, and in some cases to the twenty-eighth week, of lactation, after which there is a persistence in a high level of production for many weeks. These observations on the level of production for the individual and its high plane of maintenance over a period of time are in agreement with the observations made on women by Brodsky,[9] Laurentius [10] and Kollmann.[11] They are not in accord with the milk curves of dairy cows, in which there is a

11. Kollmann, A.: Beitrag zur Frage der Leistungsfähigkeit der Weiblichen Brustdrüse, Arch. f. Kinderh. **80**:81, 1927.

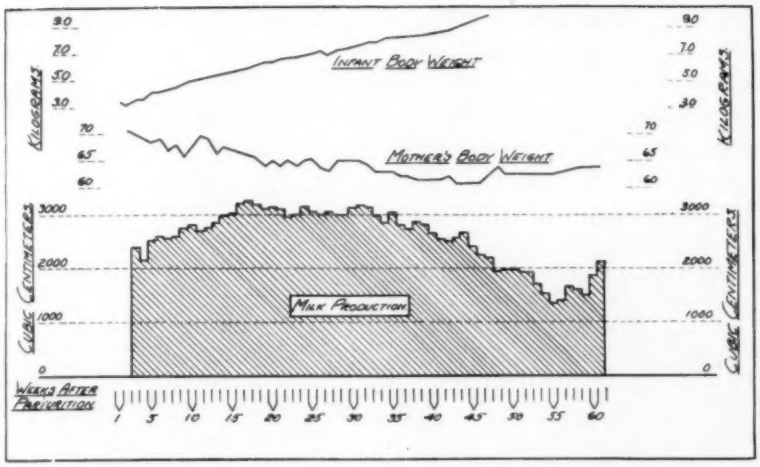

Fig. 3.—Average daily milk output in weekly intervals for subject 6 in lactation A. The entire milk supply was expressed by hand two to four times daily and quantitative measurements recorded. The weight curve of the baby who received its mother's milk by bottle is given.

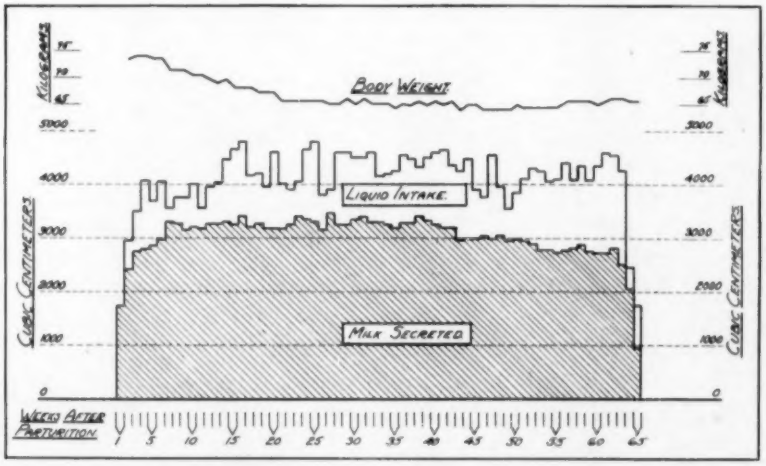

Fig. 4.—Average daily milk output and liquids drunk at weekly intervals for subject 6 in lactation B. Her weekly body weights are recorded.

characteristic tendency for milk production to reach its peak sometime during the first month post partum, followed by a gradual but persistent decline thereafter throughout the progression of the lactation period.[12] This divergence of the two curves may illustrate a physiologic difference in species.

The quantities of liquids drunk by the three women were continuously recorded during the lactation periods. Figures 4, 5 and 6 show the liquid taken as beverages alone and the amount of breast milk that was simultaneously secreted. These charts illustrate an individuality in the utilization of liquids in the production of milk. Subject 6, with a slightly lower liquid intake than her sister, subject 8, con-

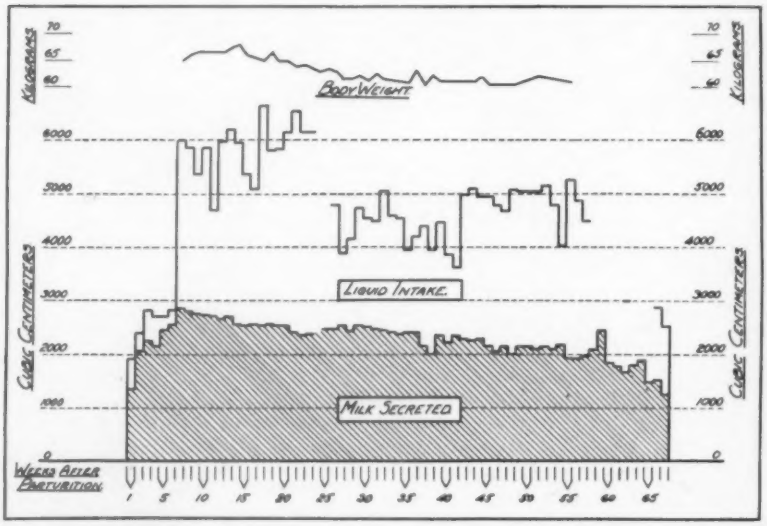

Fig. 5.—Average daily milk output and liquids drunk at weekly intervals for subject 7 in lactation B. Her weekly body weights are recorded.

tinuously produced approximately twice as much milk. Figure 3 shows the growth curve of the baby of subject 6. It is illustrative of the growth curves of all the babies, who gained from 4 to 8 ounces per week during their periods of dependence on their mothers' milk.

The maternal body weights recorded simultaneously with the milk production show a loss by subjects 6 and 7 and an appreciable gain by subject 8. Although subject 6 was losing weight, she persistently maintained her high level of milk flow. On the other hand, coincident with loss in body weight by subject 7, there was a decrease in the

12. Brody, Samuel; Ragsdale, Arthur C., and Turner, Charles W.: The Rate of Decline of Milk Secretion with the Advance of the Period of Lactation, J. Gen. Physiol. **5**:441, 1923.

quantity of milk produced. From these four summaries of milk production in women, it would seem that there is no consistent relationship between body weight and the quantity of milk flow.

The functional capacity to produce milk varies with the individual. Table 1 shows the quantities of breast milk produced by two women in a single lactation period and one woman in two successive lactation periods. The largest quantity of milk expressed at one time by subject 6 in lactation A was 2,070 cc., on the 130th day post partum, and, in lactation B, 2,340 cc. on the 222d day; in both instances sixteen hours elapsed between the emptying of the breasts. The largest amount subject 7 was able to produce at any one time in the same interval was 1,920 cc. on the 129th day of lactation. The largest amount subject

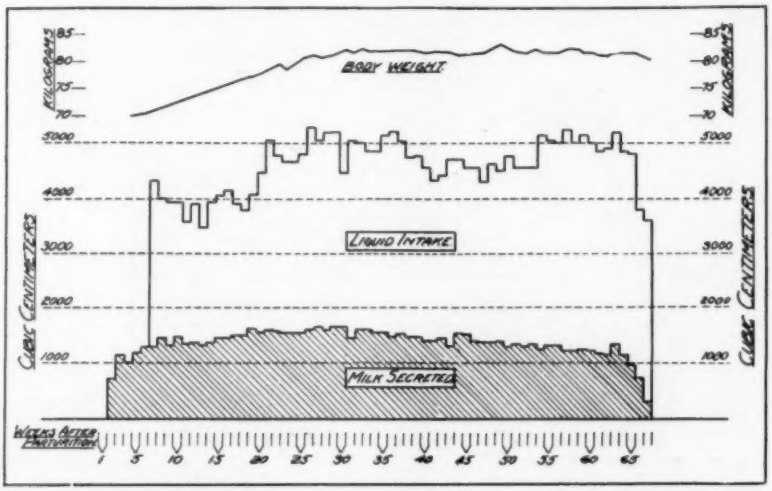

Fig. 6.—Average daily milk output and liquids drunk at weekly intervals for subject 8 in lactation B. Her weekly body weights are recorded.

8 produced at any one time was 900 cc. on the 242d day of lactation, with thirteen hours intervening between complete expressions. This subject did not have the capacity to retain milk over a longer period than thirteen hours without loss through leakage from the breasts. The highest quantities of milk expressed in a single day by these subjects were 3,390 cc. by subject 6 in lactation A, on the 98th, 154th and 165th days of lactation; by the same woman in lactation B, 4,110 cc. on the 157th day; by subject 7, 2,970 cc. on the 48th day; and by subject 8, 1,740 cc. on the 186th day of lactation. The average daily output of milk from the sixth week through the fourteenth month was 2,602 cc. for subject 6, in lactation A, and 3,134 cc. in lactation B; 2,366 cc. for subject 7; and 1,419 cc. for subject 8. It is significant to note that subject 6 did not demonstrate as great a capacity to produce milk during

lactation A as she did in the succeeding period, lactation B. With her fourth child, in lactation B, she demonstrated her greatest and most intense ability continuously to secrete large quantities of milk.

The total quantity of breast milk produced during a lactation period depends not only on the individual's immediate capacity to produce but also on the demands placed on the mammary glands and on the duration of the lactation period. Our subjects for the most part lactated for over fourteen months at their maximum capacity. During this time subject 6 produced 1,067.3 liters in lactation A and 1,454.5

TABLE 1.—*Quantities of Breast Milk Produced in Single and Successive Lactation Periods*

Subject	Descent	Age, Years	Pregnancy	Lactation	Days Post Partum When Study Started	Number of Days Followed	Total Output of Milk, Liters	Mature Milk Period*: Average Daily Output, Cc.	Mature Milk Period*: Largest Quantity Expressed in a Single Day: Amount, Cc.	Mature Milk Period*: Largest Quantity Expressed in a Single Day: Day of Lactation	Mature Milk Period*: Largest Quantity Expressed at One Time: Amount, Cc.	Mature Milk Period*: Largest Quantity Expressed at One Time: Time Since Last Expression, Hrs.	Mature Milk Period*: Largest Quantity Expressed at One Time: Day of Lactation	Body Weight at Beginning of Study, Kg.	Body Weight at End of Study, Kg.	Gain or Loss in Body Weight During Study, Kg.	Height, Cm.
6	Dutch French	25	III	A	13	411	1,067.34	2,602	3,390	98 154 165	2,070	16	130	70.8	64.0	−6.8	158
	German Danish	27	IV	B	4	450	1,454.52	3,134	4,110	157	2,340	16	222	73.1	65.8	−7.3	
7	Scotch Irish American	35	III	B	2	441	1,060.10	2,396	2,970	48	1,920	16	129	64.9	61.7	−3.2	174
8	Dutch French German Danish	29	II	B	5	458	590.94	1,419	1,740	186	900	13	242	70.4	81.7	+11.3	159

* The mature milk period is taken from the fortieth day post partum to the end of the study.

liters in lactation B; subject 7 produced 1,060.1 liters and subject 8, 590.9 liters. These quantities are not extremes, as will be evident from the following brief review of the literature on quantity milk production in women.

Among the first investigators to record studies on the capacity of women to produce milk beyond that which their own babies required were Budin in France, and Czerny and Schlossman in Germany.[9] Through special manipulation of the breasts they were able to express all the excess milk after the baby had nursed. Schlossman [13] observed that the majority of wetnurses produced more than 800 Gm. per day;

13. Schlossman, A.: Zur Frage der natürlichen Säuglingsernährung, Arch. f. Kinderh. **30**:288, 1900.

10 per cent, more than 2,000 Gm.; and 4 per cent, more than 3,000 Gm. Finkelstein [14] found that exceptional women could produce from 3,000 to 3,500 Gm., and even up to 4,000 Gm., per day, over a long period of time. Rommel [15] observed one woman who gave 4,121 Gm. in a day, and Engel [16] found some who gave from 3,000 to 4,000 Gm. daily, but the majority of his subjects gave between 1,000 and 1,500 Gm. daily. In the series of cases studied by Laurentius,[10] the majority produced daily 1,500 Gm. and more, though some produced from 2,000 to 2,730 Gm. daily. Brodsky,[9] who made a comprehensive study of seventeen wetnurses, found one woman who was able to secrete as much as 5,400 Gm. in one day. This phenomenal record in human milk production has been surpassed more recently by a woman reported by Kollmann [11] as producing as much as 5,950 Gm. of milk in one day, and as able to nurse from one to seven babies throughout fifty-one weeks of lactation.

The records just cited in the literature have all been accumulated by weighing the babies before and after nursing and quantitatively expressing the remainder of the milk. The suckling stimulus was present in all of the cases reported in these studies. In the four lactation curves presented in the present report, the suckling stimulus was entirely absent after the first few days post partum, since the babies were not allowed to nurse. The total milk supply was expressed by hand, the babies receiving their own mothers' milk by bottle. That is, the psychic effect of the suckling reflex of the child did not influence the types of milk production curves obtained in this investigation, and this study therefore demonstrates that the suckling reflex of the child is not necessary for the stimulation and continuance of heavy milk flow in women.

There seems to be little definite knowledge concerning the duration of the lactation period. In some cases it seems to be unlimited, and Engel [16] stated that: "Solange man der Saugreiz einwirken lasst, so lange dauert sie zumeist an." Cases of extremely long lactation periods have been observed; thus, von Ploss [17] reported that among the Hottentots, a people of South Africa, it is the custom of grandmothers to nurse their grandchildren. Pfaundler [18] stated that some Indian tribes nurse their children from two to twelve years, and certain tribes

14. Finkelstein, H.: Lehrbuch der Säuglingskrankheiten, ed. 2, Berlin, Julius Springer, 1921.

15. Rommel, Otto: Zur Leistungsfähigkeit der weiblichen Brustdrüse, München. med. Wchnschr. 1905, no. 10, p. 443.

16. Engel, S.: Die weibliche Brust, in Pfaundler and Schlossman: Handbuch der Kinderkrankheit, 1906, vol. 1.

17. Von Ploss: Das Kind in Brauch und Sitte der Volker, cited by Brodsky.

18. Pfaundler: Die Physiologie der Lactation, in Sommerfeld: Handbuch der Milchkunde, 1909, 117 ff.

of Eskimos, from fourteen to fifteen years. It is possible that in countries where the milk supply is inadequate and the variety of foods limited, long nursing periods are the rule. Even in this country, however, it is not uncommon to find mothers who nurse their babies for two years or more. Finkelstein [14] observed one woman who produced an average of 1,500 Gm. of milk per day for a period of nineteen months, and another who secreted 1,700 Gm. daily for twenty-five months. Schlossman [13] studied one woman who gave 4,670 Gm. in one day and averaged 3,188 Gm. daily over a period of thirteen months. Finkelstein [14] stated that he has never seen a spontaneous return of milk secretion among women who had already nursed from six to twelve months and longer. Mitchell,[19] in a study of the physiologic period of lactation in women of the United States, found that 2 per

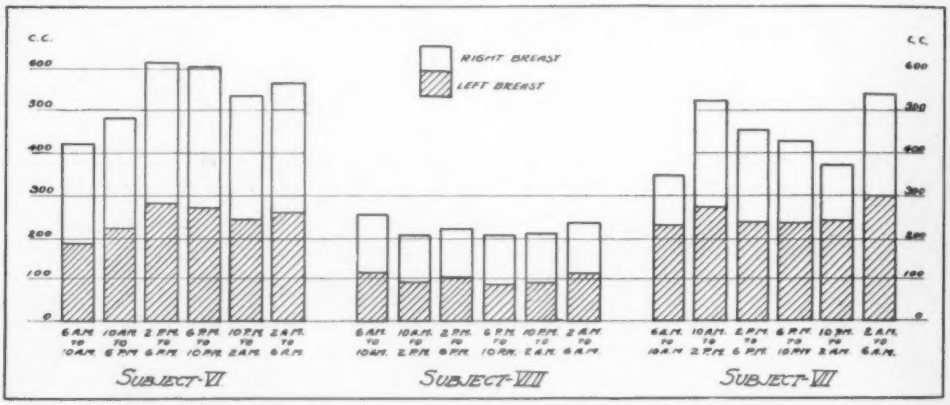

Fig. 7.—Individual fluctuations in the milk secreted by different women during a four-hour interval, the quantity output of the right and left breasts, as well as the total volume produced throughout a twenty-four-hour period (lactation A). Subject 6 had a baby 125 days of age. The mother's total twenty-four-hour output was 3,211 cc. Subject 7 had a baby 83 days of age. The mother's total twenty-four-hour volume of milk was 2,634 cc. Subject 8 had a baby 244 days of age. The mother's total twenty-four-hour volume of milk was 1,320 cc.

cent nursed their babies two years or longer. It would be of value to know more about the intensity and duration of the lactation period in the average nursing mother.

The highest point in milk production is perhaps peculiar to the individual and not to any specific time in the progression of lactation. Subject 6 reached her maximum daily output in each lactation period between the 100th and 165th day; subjects 7 and 8 attained their peaks

19. Mitchell, A. G.: The Duration of the Nursing Period in Women of the United States, J. A. M. A. **66**:1690 (May 27) 1916.

at the 48th and 186th days, respectively. The records fall within the range of the seventeen women reported by Brodsky,[9] eight of whom reached the highest point of milk production between the 43d and 80th days, seven between the 100th and 155th days, and two between the 201st and 210th days.

There are significant fluctuations in the milk secreted by individual women during a four-hour interval, in the quantity output of the right and left breasts, and in the total volume produced throughout a twenty-four-hour period (fig. 7). Table 2 illustrates some quantitative variations in volume output of the right and left breasts at intervals in a twenty-four-hour day. It is important to note that the right breast of subject 6 has a consistently greater capacity to secrete milk than has the left breast. The reverse is true for her sister, subject 8,

TABLE 2.—*Variation in Volumes of Complete Individual Four-Hour Specimen of Breast Milk Collected from the Right and Left Breasts Over an Entire Twenty-Four-Hour Period*

Time	Subject 6*			Subject 7†			Subject 8*		
	Right Breast Cc.	Left Breast, Cc.	Total, Cc.	Right Breast, Cc.	Left Breast, Cc.	Total, Cc.	Right Breast, Cc.	Left Breast, Cc.	Total, Cc.
10 p.m. to 2 a.m.	238	210	448	115	228	343	97	122	219
2 a.m. to 6 a.m.	218	192	410	250	270	520	96	102	198
6 a.m. to 10 a.m.	228	200	428	215	234	449	88	122	210
10 a.m. to 2 p.m.	221	201	422	194	230	424	100	119	219
2 p.m. to 6 p.m.	241	214	455	134	233	367	92	113	205
6 p.m. to 10 p.m.	292	262	554	236	295	531	92	113	205
Average 4-hour	240	213	453	190	248	439	97	115	208
Average 24-hour	1,438	1,279	2,717	1,144	1,490	2,634	569	691	1,250

* In the fourteenth month of lactation B.
† Study on seventy-fifth day post partum.

and also for subject 7. The relatve size of the two breasts is in each case in accord with the quantity of milk produced. Figure 8 shows the right breast of subject 6, which has the greater capacity to secrete milk, to be appreciably larger than her left breast. Similarly, the left breasts of subjects 7 and 8, the greater producers, are in each case larger than the right breasts. Figure 9 shows the different types of mammae in the three women.

Gowen and Tobey [20] have presented data to show that the size of the udder measures closely the amount of milk which the cow is able to secrete. Their results indicate that about one fifth of a pound of secreting tissue is necessary for the secretion of a pound of milk during a period of fifteen hours. Assuming that the processes of milk secretion are the same in all mammals, and that the flow of milk is somewhat constant throughout a twenty-four-hour period, then at the maximum

20. Gowen, J. W., and Tobey, E. R.: Udder Size in Relation to Milk Secretion, J. Gen. Physiol. **10**:949, 1927.

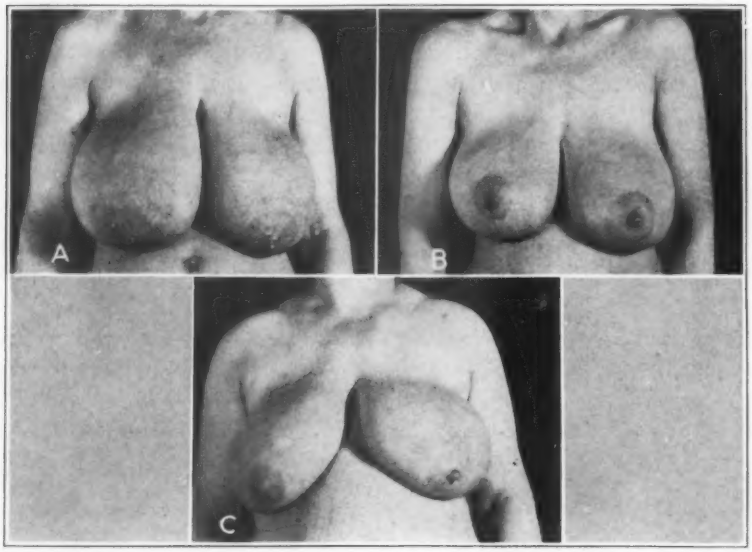

Fig. 8.—*A* shows the breasts of subject 6; *B*, of subject 7 and *C*, of subject 8.

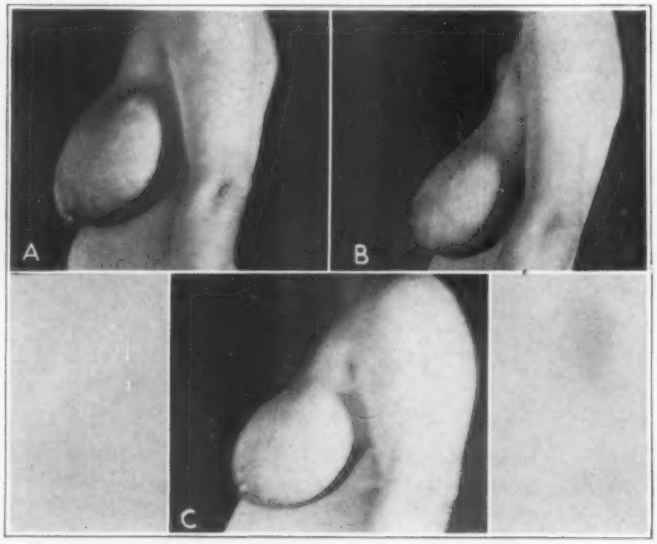

Fig. 9.—The different types of mammae in three women: *A*, subject 6; *B*, subject 7; *C*, subject 8.

period of milk production the amount of active secreting mammary tissue for the three women would roughly approximate 0.514 Kg. for subject 6, 0.371 Kg. for subject 7 and 0.219 Kg. for subject 8.

In measuring the amount of milk expressed, one cannot tell whether one is measuring the rate of formation of milk or merely the rate of outpouring of preformed secretory constituents. Table 2 shows the total amount of milk that the breasts of the three women are capable of elaborating over a four-hour interval, while table 1 shows the maximum quantities of milk produced by the individual women over thirteen- and sixteen-hour intervals. These records demonstrate the marked capacity of the mammary glands to store milk or its precursors, or both.

Swett, Graves and Miller,[21] in their study of the comparison of the conformation, anatomy and skeletal structure of a highly specialized dairy cow and a highly specialized beef cow, found that in the beef cow the udder was more compact and more closely attached, with less looseness, greater width and less depth, as compared with that of the dairy cow. Figure 8 shows that these comparative characteristics hold true for the mammary glands of the women observed in this investigation. Thus, subject 8, who was the smallest producer, had much more compact breasts than either of the other two subjects. Swett, Graves and Miller, in studying the gross anatomy of the udders by means of their vertical transverse sections, found in the dairy type, as contrasted with the beef type, indications of the presence of more glandular tissue, together with large ducts or cisterns and an almost complete absence of fat. The fact that subjects 6 and 7 have loose, long, fibrous mammary glands and a unique capacity to store excessive quantities of milk or its precursors over a sixteen-hour period would tend to indicate the presence of less fat in their breasts and of large galactophores and lactiferous sinuses which serve as temporary reservoirs. In contrast, subject 8 has not only more compact and firmer breasts but also an inability to retain milk in large quantities beyond a period of thirteen hours, which indicates that she has not only more fat and less parenchymal tissue, but also a smaller amount of stroma and fewer galactophorous sinuses in her mammae.

The modus operandi of human milk flow is by no means completely understood. The rôle of heredity in human milk secretion has been studied to some extent,[22] but more information is needed. Our three subjects, two of whom are sisters, come from families in which satisfactory breast feeding is the rule. They have, in each case, a

21. Swett, W. W.; Graves, R. R., and Miller, F. W.. Comparison of Conformation, Anatomy, and Skeletal Structure of a Highly Specialized Dairy Cow and a Highly Specialized Beef Cow, J. Agric. Research **37**:685, 1928.

22. Winternitz, Ida: Erhebungen und Betrachtungen über Stillfähigkeit, Arch. f. Kinderh. **71**:109, 1922.

widely varied racial descent (table 1). Although the body constitutions and the psychophysical types of these mothers are being considered, we are unversed in the significance of these factors in human milk secretion. The ages of the women range between 25 and 35 years, but whether or not age has any bearing on the ability of a woman to produce milk is a question. Menstruation is said to have a determinate influence on milk secretion.[23] Consideration is being given to this physiologic factor.

Within limits, the quantity of milk secreted by physiologically normal mammary glands adjusts itself to the demand. The removal of milk from the breasts encourages secretion, whereas the accumulation of milk discourages it.[24] When a greater demand is placed on the mammary glands, the quantity of milk output is increased. This increase in output can be accomplished by placing another child on the breast, or by expressing the excess milk and completely emptying the breasts at frequent intervals, either by hand or by breast pump. This stimulation of an increased flow of milk by a complete expression after nursing can be demonstrated soon after delivery, as well as throughout the whole of the lactation period. Rosenfeld[25] has pointed out (table 3) the effectiveness of complete removal of the milk from the breasts at the nursing intervals, beginning immediately after delivery.

TABLE 3.—*Increase in Volume of Milk When Breasts Are Completely Emptied (After Rosenfeld)*

	Days							
	1	2	3	4	5	6	7	8
Normal amount of daily consumption according to Jachke	20	85	172	252	322	375	411	436
Average daily consumption of our children	49	168	254	325	367	426	424	...
Milk produced (drunk and expressed)	55	205	345	456	474	521	530	...

It will be noted that the milk production is appreciably increased when the milk is expressed after nursing, thus completely emptying the breasts at frequent intervals.

Frequent and thorough stripping of the breasts seems to be effective in producing notable increases in the output of milk at any stage of lactation. Figure 10 illustrates the stimulation of an increased output of breast milk over a period of four or five days by a complete emptying of the breasts at five instead of the usual two or four times per day,

23. Marshall (footnote 5, second reference).

24. Moore, C. Ulysses: Nutrition of Mother and Child, Philadelphia, J. B. Lippincott Company, 1923.

25. Rosenfeld, W.: Die Milchbeshaffung für die Ernährung lebensschwacher Neugeborener mit konserviertir Frauenmilch nach Meyerhofer und Pribram, Wien. klin. Wchnschr., 1909, no. 29, p. 1038.

at the sixth week, and at the sixth, ninth and fourteenth months of the lactation period. Further confirmatory evidence is given in figure 3, which shows that the output of milk decreased when there was less stimulation but increased markedly after reestablishment of more frequent stimulation. Another striking example is shown in the case of subject 7, in whom decreased stimulation late in lactation A resulted in a depression of the quantity output of milk to only 300 cc. daily. By means of pumping the breasts dry from three to five times daily, the quantity output was tripled in ten days.

Table 4 shows the volume output of breast milk at definite intervals throughout the twenty-four-hour day when the collections were made

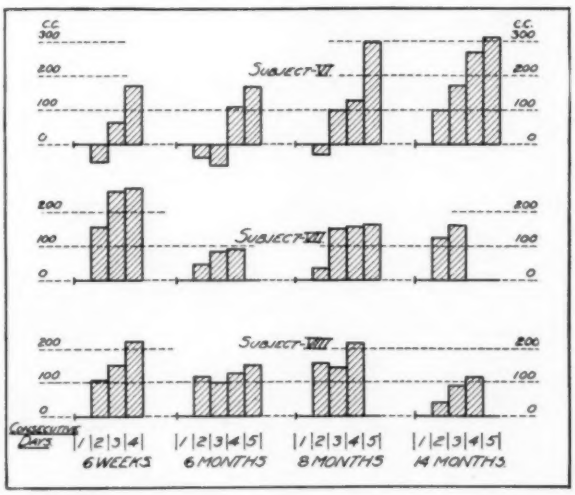

Fig. 10.—Chart showing the increased output of breast milk over a period of four or five days stimulated by complete emptying of breasts five, instead of the usual two to four, times per day. The basal line represents the milk output on the first day of the stimulation period; the increases or decreases from this level are recorded daily thereafter.

over a continuous ten-day period. Previous to this study, subjects 6 and 7, respectively, in lactation A, were accustomed to expressing their milk two times daily. When the breasts were emptied five or six times daily, there was a marked increase from day to day. Subject 6 augmented her daily production 593 cc. and subject 7, 403 cc. in the ten-day period. It took from seven to eight days to reach a high plane of milk production after frequent stimulation was inaugurated. Therefore, if increased flow does not start immediately (fig. 7, subject 6) after the initiation of more frequent and complete emptying of the breasts, persistence of rhythmic stimulation should be maintained throughout at least ten days before hopes of augmented milk produc-

tion are lost. These observations are in accord with clinical observations.[26] Table 4 shows not only the fluctuations in the amounts of milk secreted over four-hour intervals throughout the twenty-four-hour day, but also a gradual increase in the mean four-hour output. It shows also the maximum variations of milk secreted at four-hour intervals over a continuous period of two hundred and forty hours.

These results again demonstrate that if augmented milk production is desired, all the milk should be removed from the breasts at regular intervals and as completely as possible. The number of times daily that the milk should be removed may vary with the individual.

There are additional important influences on milk secretion. The amount of protein in the average voluntary food intake of the three women varied between 162 and 168 Gm., and the daily calories from 3,900 to 4,600. These figures are based on consecutive five- to ten-day studies of weighed dietaries at different intervals in two successive lactation periods.

Moderate exercise reduces the flow of milk and intensive exercise has an unfavorable influence on the amount and kind of milk produced.[27] Our observations on these three women subjects show that excessive exercise and heavy work do tend to depress maximum quantity output of milk. A quantitative evaluation of the intensity of the work has been recorded but not yet interpreted.

Nervous factors, such as excitement, fear and anxiety, are known to suppress the flow.[28] Severe shock may cause a complete cessation of milk secretion.[29] The effect of emotional disturbances is being considered.[8]

The psychophysical type of the individual may play an important rôle in determining the ability to secrete milk. Medical or clinical experience has led to the opinion that the nervous, high-strung woman is not a satisfactory milk producer. Is it not possible, however, that the clientele of the majority of physicians is made up of women who are failing in milk secretion, or who are disturbed because of other reasons, and that physicians have therefore not had an opportunity to study intensively, over long periods of time, women who are producing satisfactory quantities of milk?

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26. Sedgwick, J. P.: Establishment, Maintenance, and Reinstitution of Breast Feeding, J. A. M. A. **69**:417 (Aug. 11) 1917. Moore (footnote 24).

27. Heineman, Paul G.: Milk, Philadelphia, W. B. Saunders Company, 1921. Turner, William A., and Hartman, A. M.: Calcium and Phosphorus Metabolism in Dairy Cows: III. The Adequate Ration for High-Producing Cows and the Effect of Exercise on Calcium, Phosphorus and Nitrogen Balance, J. Nutrition **1**:445, 1929.

28. Vincent, Ralph: Nutrition of the Infant, New York, William Wood & Company, 1904, p. 47.

29. Smith, Thomas C.: Sudden Suppression of Milk Due to Fright, Am. J. Obst. **45**:89, 1902.

TABLE 4.—*Volume Output of Breast Milk at Definite Intervals Throughout the Twenty-Four-Hour Day When Collections Were Made Over a Continuous Ten-Day Period*

Demonstrating an Increased Milk Production Through Complete and Regular Emptying of Breasts

Day of Study	Interval Between Collections: Time of Day	Hours Elapsing	Volume Production: Subject 6* — Interval Output: Amount, Cc.	Interval Output: Average 4 Hour, Cc.	Interval Output: Maximum Variation in 4 Hour, Cc.	Complete 24 Hour Specimen: Total, Cc.	Complete 24 Hour Specimen: Increase‡ Cc.	Subject 7† — Interval Output: Amount, Cc.	Interval Output: Average 4 Hour, Cc.	Interval Output: Maximum Variation in 4 Hour, Cc.	Complete 24 Hour Specimen: Total, Cc.	Complete 24 Hour Specimen: Increase‡ Cc.
1	6 a.m.-10 a.m.	4	250					155				
	10 a.m.- 2 p.m.	4	237					132				
	2 p.m.- 6 p.m.	4	264					172				
	6 p.m.-10 p.m.	4	285					168				
	10 p.m.- 6 a.m.	8	524	260	48	1,560	0	320	158	40	947	0
2	6 a.m.-10 a.m.	4	270					166				
	10 a.m.- 2 p.m.	4	280					160				
	2 p.m.- 6 p.m.	4	286					192				
	6 p.m.-10 p.m.	4	284					162				
	10 p.m.- 6 a.m.	8	556	266	16	1,676	116	340	170	36	1,020	73
3	6 a.m.-10 a.m.	4	278					180				
	10 a.m.- 2 p.m.	4	282					180				
	2 p.m.- 6 p.m.	4	290					180				
	6 p.m.-10 p.m.	4	346					218				
	10 p.m.- 6 a.m.	8	580	296	68	1,776	216	350	185	43	1,108	161
4	6 am.-10 a.m.	4	315					187				
	10 a.m.- 2 p.m.	4	252					170				
	2 p.m.- 6 p.m.	4	332					180				
	6 p.m.-10 p.m.	4	323					240				
	10 p.m.- 2 a.m.	4	338					110				
	2 a.m.- 6 a.m.	4	310	312	80	1,870	310	278	194	168	1,165	218
5	6 a.m.-10 a.m.	4	286					174				
	10 a.m.- 2 p.m.	4	289					186				
	2 p.m.- 6 p.m.	4	355					202				
	6 p.m.-10 p.m.	4	345					220				
	10 p.m.- 2 a.m.	4	370					189				
	2 a.m.- 6 a.m.	4	308	326	84	1,953	393	225	199	51	1,196	249
6	6 a.m.-10 a.m.	4	275					170				
	10 a.m.- 2 p.m.	4	289					190				
	2 p.m.- 6 p.m.	4	322					225				
	6 p.m.-10 p.m.	4	352					242				
	10 p.m.- 2 a.m.	4	356					199				
	2 a.m.- 6 a.m.	4	344	323	81	1,938	378	232	210	72	1,258	311
7	6 a.m.-10 a.m.	4	340					186				
	10 a.m.- 2 p.m.	4	330					206				
	2 p.m.- 6 p.m.	4	348					250				
	6 p.m.-10 p.m.	4	386					210				
	10 p.m.- 2 a.m.	4	377					...				
	2 a.m.- 6 a.m.	4	341	354	56	2,122	562	452	217	64	1,304	357
8	6 a.m.-10 a.m.	4	394					204				
	10 a.m.- 2 p.m.	4	274					199				
	2 p.m.- 6 p.m.	4	342					208				
	6 p.m.-10 p.m.	4	338					237				
	10 p.m.- 2 a.m.	4	...					213				
	2 a.m.- 6 a.m.	4	712	343	120	2,060	500	230	216	38	1,297	350
9	6 a.m.-10 a.m.	4	358					200				
	10 a.m.- 2 p.m.	4	308					205				
	2 p.m.- 6 p.m.	4	380					208				
	6 p.m.-10 p.m.	4	356					202				
	10 p.m.- 6 a.m.	8	728	355	72	2,130	570	422	216	62	1,297	350
10	6 a.m.-10 a.m.	4	376					234				
	10 a.m.- 2 p.m.	4	280					250				
	2 p.m.- 6 p.m.	4	371					208				
	6 p.m.-10 p.m.	4	400					242				
	10 p.m.- 6 a.m.	8	726	359	120	2,153	593	416	225	42	1,350	403

* The study of subject 6 was carried out Dec. 1-11, 1927, beginning on the 413th day post partum.

† The study of subject 7 was carried out Oct. 24 to Nov. 2, 1927, beginning on the 338th day post partum.

‡ The initial output on the first day of the study was taken as the base line.

SUMMARY

1. Lactation has been shown to persist at a high level over fourteen months in the total absence of the suckling reflex. The total quantity of milk produced in this period has been recorded during two successive lactation periods of one woman, and during a single period for two other subjects.

2. There are significant variations in the volume output of milk of individual women from hour to hour and from day to day. Such fluctuations may have an appreciable influence on the nurturing of the average breast-fed infant.

3. There is a definite individual functional capacity for producing milk at a given time in the lactation period.

4. Frequent and complete emptying of the breasts encourages milk flow.

PHENYLETHYLHYDANTOIN IN THE TREATMENT OF SYDENHAM'S CHOREA *

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Phenylethylhydantoin was introduced under the name "nirvanol" [1] in 1916 as a sedative. The frequent occurrence of severe symptoms such as rash or fever led many authors [2] to warn against its use. In 1919, Roeder [3] recommended phenylethylhydantoin in the treatment for chorea minor.

The reports [4] were so encouraging that we undertook a study of the action of this drug in a series of cases of chorea. Since chorea is a highly variable disease, no therapeutic study is convincing unless a fairly large number of cases is included, and unless comparison is made with cases in the same series in which the patients were treated by other methods. So far as we are aware, this has not been done previously. This report is based on the study of twenty-five cases; as the children entered the hospital, every other one was treated with phenylethylhydantoin. The dose for younger children was 0.3 Gm. (5 grains) per day; for the older children, 0.6 Gm. (10 grains); the drug was given for from seven to nine days. Treatment in the alternate cases varied somewhat (table 2).

RESULTS

"Nirvanol Sickness."—The sedative effects of phenylethylhydantoin usually appear on the second or third day of its administration. Fever usually develops on the seventh day, reaches a maximum on the ninth day and subsides on the eleventh day. The use of the drug was usually discontinued when fever or rash appeared; fever can be prolonged if the drug is continued. On the ninth day, a few reddish-brown maculopapules appear on the thighs, wrists or abdomen, the face often appears swollen and flushed, and a pale pink exanthem may appear on the soft palate or buccal mucosa. By the next day or two, the exanthem [figs. 2 and 3] has become general. It is usually distinctly morbilliform but somewhat more like urticaria than the rash of measles. Itching may be intense. Occasionally, the rash is punctate and resembles that of

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* Prof. Treat B. Johnson has undertaken the synthesis of homologues of phenylethylhydantoin, which are to be used in the further study of this problem.

TABLE 1.—*Phenylethylhydantoin in Chorea*

Type of Chorea	Case	Sex	Age, Years	Medication: Dose per Day	Medication: Days Given	Medication: Total	Fever: Onset After Beginning Drug, Days	Fever: Duration, Days	Fever: Maximum Temperature, C.	Eruption: Onset After Beginning Drug, Days	Eruption: Duration	Eruption: Type†	Duration of Chorea in Days: A Before Treatment Began	Duration of Chorea in Days: B To Most Rapid Improvement From A	Duration of Chorea in Days: C From Beginning of Treatment to Recovery	Duration of Chorea in Days: D Entire Duration	Subsequent History: Reexamined After Treatment, Months	Subsequent History: Recurrences
Severe	1	F	7	0.3	8	2.4	9	3	39.5	10	8	M	42	11	22	64	18	None
Severe	2	F	5	0.3	5	1.5		No fever		5	3	M	3	9	14	17	8½	None
Severe	3	F	12	0.3-0.5	7	2.7	6	9	40.5	7	8	M	1	15	20	21	9	None
Severe	4‡	F	11	0.3-0.5	24	10.2	8	1	37.9	9	6	M	56	14	36	92	8½	None
Severe	5	F	9	0.5	9	4.5	7	6	39.5	9	8	M	10	11	15	25	8	None
Severe	6	F	10	0.5	10	5.0	9	5	38.5	10	7	M	5	12	24	29	7½	None
Average			9		10.5	4.4	8	5		8	7		19.5	12	21.8	41.3	9.9	
Moderate	7§	M	10	0.3	6	1.8	8	1	39.1	8	10	M,U,S	7	14	56	63	17	2
Moderate	8#	M	4	0.3	11	3.3	5	1	38.9	5	3	S,U,M	7	15	19	26	11	1
Moderate	9	F	10	0.3	8	2.4	8	6	40.0	9	7	M	6	11	53	59	12	None
Moderate	10¶	F	7	0.3-0.5	19	7.1	7	7	38.8	7	4	M,U	28	25	42	70	4	None
Moderate	11	M	7	0.5	11	5.5		No fever			No rash		62	15	23	85	9	1
Average			7.6		11	4.0	7	4		8	6		22	16	38.6	60.6	10.6	
Mild	12	F	12	0.3-0.5	11	3.7	12	4	37.8	11	6	M	14	9	65	79	9½	None
Mild	13	M	9	0.5	9	4.5	7	6	40.5	10	3	M	34	12	17	51	7½	None
Average			10.5		10	4.1	9	5		10	4		24	10.5	41	65	8.5	
Average all cases			8.7		10.5	4.2	7.8	4.5		8.5	6.3		21	13.3	31 ± 3.1	52 ± 4.7	9.8	

† M indicates morbilliform; U, urticarial; S, scarlatiniform.
‡ No. 4 received a second course of treatment.
§ No. 7 had morbilliform and urticarial eruption with leukopenia after three doses of phenylethylhydantoin, a scarlatinal eruption with leukocytosis three hours after the fourth dose and no further reaction after two more doses.
# No. 8 had a scarlatiniform and urticarial eruption after five daily doses; subsequently had a morbilliform eruption after a second course of five daily doses.
¶ No. 10 had no rash or fever after twelve daily doses of 0.3 Gm., but had a morbilliform rash after a second course of seven daily doses of 0.5 Gm.

scarlet fever. Leukopenia was observed in eight of nine cases. Leukocytosis occurred (— 15,400; 26,600 —) in the two patients with scarlatiniform rash. A marked eosinophilia was observed in all the specimens of blood that were studied during the eruption.

In one case fever but no rash appeared; in one, neither rash nor fever. The latter child developed delirium, which continued for three days.

TABLE 2.—*Drugs Other than Phenylethylhydantoin in Chorea*

Type of Chorea	No.	Sex	Age	Drugs	Duration of Chorea, Days: Before Treatment	Duration of Chorea, Days: From Beginning of Treatment to Recovery	Duration of Chorea, Days: Total	Subsequent History: Reexamined After Treatment, Months	Subsequent History: Recurrences
Severe....	14	F	11	Phenylethyl barbituric acid; ether in oil (by rectum); salicylates	14	98	112	21½	2
Severe....	15	F	14	Phenylethyl barbituric acid; ether in oil (by rectum); salicylates	28	54	82	19	None
Severe....	16	F	11	Salicylates; ketogenic diet	1	389	390	10	Died, carditis
Average, severe.....	12				14	180	195	16.6	
Moderate	17	F	10	Phenylethyl barbituric acid; salicylates	7	35	42	3	None
Moderate	18	M	12	Phenylethyl barbituric acid	84	35	119	14	1
Moderate	19	F	14	Solution of potassium arsenite	10	123	133	5	None
Average, moderate..	12				34	61	98	7.3	
Mild.....	20	M	12	Solution of potassium arsenite	21	99	120	17	None
Mild.....	21	F	8	Phenylethyl barbituric acid	1	105	106	26	None
Mild.....	22	M	4	Phenylethyl barbituric acid	42	61	103	13½	1
Mild.....	23	F	12	Salicylates	28	176	204	6	1
Mild.....	24	F	14	Salicylates	2	90	92	4	None
Average, mild.....	10				18.8	106	125	12.6	
Average of all.....	11				21.7	115 ± 19.4	137 ± 18.1	12.4	

In none of our cases did any permanently harmful effects develop. Harmful effects from nirvanol as reported are: agranulocytosis,[5] hemorrhagic nephritis with death,[6] delirium,[7] dyspnea associated with swelling of the tracheobronchial lymph nodes [8] and the discomfort incident to the usual reaction. The nephritis was obviously not due to nirvanol but to streptococcal infection, proved at autopsy.

Influence on Chorea.—The primary sedative action of phenylethylhydantoin in chorea is usually slight. When the characteristic "nirvanol sickness" appears, choreic manifestations become exaggerated. When the rash and fever begin to disappear, choreic symptoms rapidly become

less. The subsequent duration of the disease is apparently greatly shortened. As the same person studied all of the cases, it would appear that the observations in the two series of cases are comparable. These facts, as observed in our cases, are presented in table 1 and figure 1. The data for eleven control cases are presented in table 2.

As will be observed in table 2, the control series may not seem strictly comparable to the series in which phenylethylhydantoin was used. Case 16 is of unusually long duration. Even if case 16 is omitted from the series (which omission we do not think justifiable), the average duration of the cases in this series becomes eighty-eight days from the time of beginning treatment.

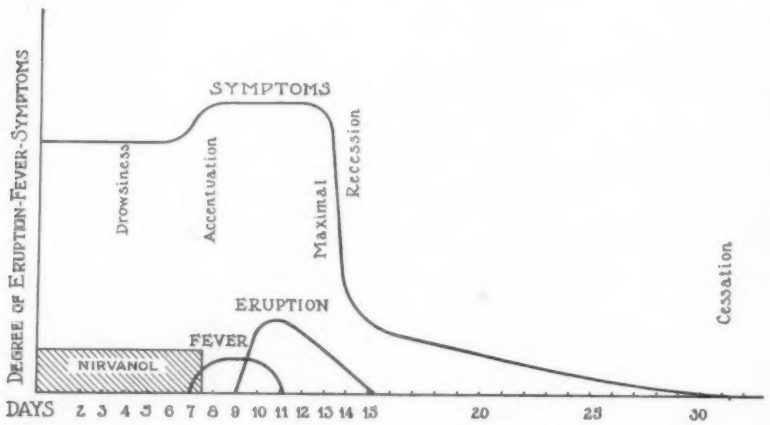

Fig. 1.—Chart showing the influence of "nirvanol sickness" in chorea. Time of onset and duration of fever and rash are the averages observed in thirteen cases. The degree of fever and rash and the intensity of the rash and choreic symptoms are expressed in arbitrary units.

We are, of course, aware that the duration of symptoms in chorea cannot be judged to a period as short as a day. We have, however, for purposes of statistical analysis, used the figures as given in the tables for calculating the "probable error" of the mean duration by the usual formula:

$$\text{P.E.} = 0.675 \sqrt{\frac{\Sigma (M - x)^2}{n (n - 1)}}$$

Where M is the mean, x is any one of the data, and n is their number.

The mean duration of chorea from the beginning of treatment until "cure" in patients not receiving phenylethylhydantoin was 115 ± 19.4 days; in cases in which the patients were treated with phenylethylhydantoin, the mean duration was 31 ± 3.1 days. The difference of these means is 84 ± 19.7 days. This difference is significant because

Fig. 2.—"Nirvanol sickness;" edema of the face. The rash resembles serum sickness.

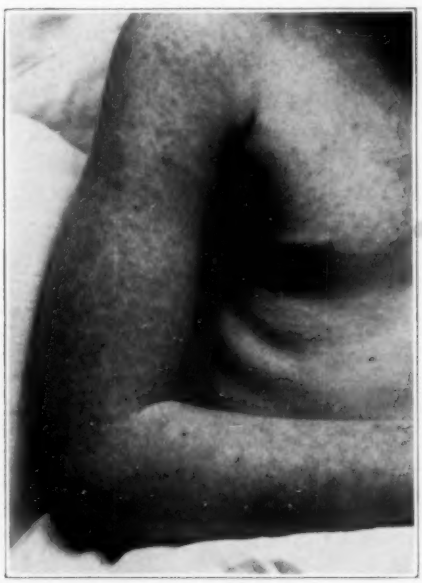

Fig. 3.—"Nirvanol sickness;" maculopapular and urticarial rash.

it is more than three times its own probable error; in fact, it is four and three-tenths times its probable error.

In the same way, it can be shown that the entire duration of chorea, from the onset of symptoms until cure, is shortened by the use of phenylethylhydantoin by 84 ± 18.7 days, again a significant difference.

Our observations suggest the following conclusions: Treatment with phenylethylhydantoin greatly shortens the course of Sydenham's chorea. This effect is more obvious in the more severe cases. The recurrence of chorea is no more frequent after the administration of phenylethylhydantoin than after other forms of treatment. In two cases active carditis was not aggravated by the treatment. The beneficial results did not always seem to depend on the development of fever or rash.

On the basis of this small series of cases, no claim can be made that all patients with chorea will respond to the treatment. The relatively poor response in mild cases strongly suggests that many will not.

COMMENT

The mechanism of "nirvanol sickness" is obscure. Nothing similar has been observed in animals. In rabbits, large doses (from ten to twenty times that used in man) led to exhaustion of the bone-marrow and agranulocytosis. Feer [5] observed the case of a boy who received the usual doses of nirvanol for chorea; he developed the alarming syndrome of agranulocytic angina; he eventually recovered. Caution must therefore be observed not to administer the drug over periods longer than ten days, and to follow the blood count in all cases. We doubt that eosinophilia is a necessary concomitant of improvement. The close analogy between measles and reactions to phenylethylhydantoin suggests the possibility that anergy may play a rôle in the improvement of choreic patients.

No studies are reported concerning the localization of phenylethylhydantoin in the nervous system, or concerning its elimination from the body. The fact that phenylethyl barbituric acid, which resembles phenylethylhydantoin in structure, appears to be localized [9] exclusively in the thalamus and corpus striatum and not in the other nervous tissue, suggests that phenylethylhydantoin may become localized in the same region, and may thus have a direct effect on the parts of the brain supposed by some to be affected in chorea.

It is probable that phenylethylhydantoin is not the best drug of the hydantoin series for use in the treatment for chorea.

CONCLUSIONS

1. Phenylethylhydantoin proved in our experience more effective than other drugs in the treatment for chorea. In the present com-

parative study, the mean duration of chorea from the beginning of treatment was thirty-one days when phenylethylhydantoin was used, and one hundred and fifteen days when other drugs were used.

2. Mild chorea is not so rapidly cured as is the severe form.

3. Although "nirvanol sickness" may cause considerable temporary discomfort, we have observed no permanent harmful effects from the drug.

4. On account of the possible danger of injury to the bone-marrow, it is desirable that frequent blood counts be made in cases in which patients with chorea are treated by phenylethylhydantoin.

5. The administration of the drug should not be continued over periods longer than ten days, or after the appearance of the eruption.

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RELATIVE PROPHYLACTIC VALUE OF CONVALESCENT AND IMMUNE ADULT MEASLES SERUMS*

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The prophylactic use of convalescent serum for the prevention of measles among children exposed to the disease has been reported by various investigators. The protective value of this agent seems unquestionable. The use of immune serum and whole blood from children or adults who have had an attack of the disease several years previously has also been advocated, but little evidence has been advanced as to the exact value of this agent.

During the last four months of the year 1928 and the early part of 1929, we had the opportunity to test the value of convalescent and immune adult serums, in various doses, among children in Porto Rico exposed to the disease by familial contact. One hundred and twenty doses of convalescent serum and 393 doses of immune adult serum were administered to more than 500 children, over 6 months and under 15 years of age, who had not previously had the disease and who were exposed to a case of measles in the same house at the time of immunization. In addition, 183 children living in the same houses with these patients and with the immunized children and who had not had the disease were left as controls and observed together with the immunized group during a period of eight weeks following exposure.

In testing the relative value of immune adult serum, we aim chiefly to give the general practitioner the true value of a prophylactic agent which is readily available.

We have seen only five reports in the American literature on the subject of immune adult serum. Godfrey,[1] in his report of the results obtained with convalescent serum in New York State Institutions, mentioned that of 38 children immunized with serum from adults who have had the disease, 21 developed measles. Ten of the 17 who received injections who did not develop the disease were found to have had measles previously in the institution. This leaves only 7 of those into whom injections were made who received complete protection. The

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* Read at the Annual Meeting of the Porto Rico Medical Association, San Juan, Dec. 20-24, 1929.

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amount of immune serum used in this experiment is not given. In the same paper, the author reported the use of doses of 4 cc. of immune adult serum in 5 children 3 years of age. Two of the 5 developed measles. Six of 7 controls developed measles. If similar amounts of adult serum were used in the experiment reported previously, the small proportion of children protected seems to be explained if the serum used by this investigator was similar in strength to that used in our experiment.

Bivings [2] employed amounts varying from 8 to 25 cc. of adult immune serum. Three of 9 children immunized escaped, and 6 developed a modified attack of the disease. In a later experiment, Bivings and Dickson [3] reported complete protection in 12 of 23 children into whom injections were made and attenuated measles in the remaining 11.

Zingher [4] reported that serum from adults who have had an attack of measles during childhood will protect against an attack of the disease. He further stated that somewhat larger amounts have to be used. The author presented no data, however, as to the number of children immunized with this serum. Karelitz and Levin [5] reported the use of adult serum and whole blood in 14 children, 3 of whom developed measles. Two of these, however, were given blood from adults who had never had the disease.

There are a number of experiments reported in the literature by investigators from abroad relative to the value of immune adult serums. Bader,[6] in his review of the foreign literature, quoted the work of the following investigators. Kutter [7] reported its use in 15 children with only one failure. Salomon [8] used 10 and 15 cc. of this serum and reported complete protection in 36 of 72 children receiving injections. Von Torday [9] immunized with adult serum the largest number of persons on record and reported only 12 failures in 116 injections. He used 20 cc. of adult serum from the second to the sixth day of exposure.

PROCEDURE

Convalescent measles serum employed in the present experiment was obtained from patients admitted to the Quarantine Hospital at San Juan, Porto Rico, during

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the early part of 1929 with a diagnosis of measles. The serum was invariably obtained from the fifth to the tenth day of convalescence. The immune serum was obtained from inmates at two charitable institutions of the Insular Department of Health at San Juan. It was obtained from only persons who had an attack of measles more than one year and less than ten years from the day the blood was withdrawn. A history of a previous attack of measles among these children was obtained from the hospital records of these institutions.

Both convalescent and immune serums were prepared as follows: Under strict aseptic conditions, blood was withdrawn from a vein in the forearm into a sterile flask, quantities ranging from 100 to 500 cc. being collected, depending on the size and physical condition of the donors. The flask was stoppered with its sterile plug and the blood allowed to coagulate; the clot was then run off from the sides of the flask with a sterile pipet and the flask placed in the icebox for from twelve to twenty-four hours. The serum was then pipetted off. Similar batches of serum were pooled, centrifugated at high speed for three minutes and the clear serum pipetted off and dispensed in appropriate serum bottles. Enough 5 per cent phenol solution in physiologic solution of sodium chloride was added to bring the final concentration of the serum to 0.5 per cent, in the proportion of 1 part of the 5 per cent phenol to 9 parts of serum. Sterility tests were made for each batch of serum. During the whole process, as sterile a technic as possible was maintained. The serum was then kept in the icebox until used, no serum being kept there more than two months after the time of its preparation. A Wassermann test of the blood and a careful search for malarial parasites in the blood were made on all donors before their blood was used.

Two sanitary inspectors and two nurses made a daily house to house canvass in three communities chosen for the experiment. All cases suspected of being measles were located and were then seen by one of us (Garrido Morales) for the purpose of diagnosis. The cases of children between the ages of 6 months and 15 years who had no history of a previous attack of measles and were living in intimate contact with the patients with the disease were recorded. Every third child was regarded as a control and received no treatment, while each of the remainder received an injection of either convalescent or immune serum.

Subsequent visits at intervals of from two to four days were made by the inspectors to these houses for a period of eight weeks, and any illness noted among the children who received injections or among the control group was reported to one of us (Garrido Morales), who visited the patient immediately to determine the cause of illness and, if measles, the severity of the disease.

RESULTS

Table 1 shows the total number of children exposed to measles by familial contact and immunized with convalescent or immune adult serum, the number left as controls, and the number and percentage who did not develop measles among each group.

Table 2 classifies by age groups the total number of children immunized with convalescent or immune adult measles serum and gives the number and percentage protected, also the number who did not receive treatment with serum (controls) and the number and percentage who escaped among this group.

Table 3 presents the results obtained by the use of different amounts of convalescent and adult serum among children exposed to the disease.

TABLE 1.—*Relative Value of Convalescent and Immune Serums*

Type of Serum Administered	Total Number Exposed and Immunized, with Controls	Did Not Develop Measles	
		Number	Per Cent
Convalescent	120	102	85.0
Immune adult	393	227	57.8
No serum (controls)	183	34	18.6

TABLE 2.—*Total Treated and Untreated Children, with Number and Percentage Who Did Not Develop Measles, Classified by Age Groups*

Type of Serum	Age Groups	Total Exposed and Immunized with Controls	Did Not Develop Measles	
			Number	Per Cent
Convalescent	6 months to 4 years	63	51	81.0
	5 to 9 years	41	37	90.2
	10 to 14 years	16	14	87.5
	All	120	102	85.0
Immune adult	6 months to 4 years	212	111	52.4
	5 to 9 years	146	91	62.3
	10 to 14 years	35	25	71.4
	All	393	227	57.8
No serum (controls)	6 months to 4 years	96	7	7.3
	5 to 9 years	66	15	22.7
	10 to 14 years	21	12	57.1
	All	183	34	18.6

TABLE 3.—*Results Obtained with Different Amounts of Convalescent and Immune Serums*

Serum Administered		Total Number Exposed and Immunized	Received Complete Protection	
Type	Amount, Cc.		Number	Per Cent
Convalescent	4	13	9	69.2
	5	46	38	82.6
	6	61	55	90.2
All		120	102	85.0
Immune adult	10	138	56	40.6
	15	123	65	52.8
	20	70	54	77.1
	30	34	28	82.4
	40	28	24	85.7
All		393	227	57.8

TABLE 4.—*Days After Immunization that Measles Rash Developed*

Number of Days	Type of Serum Injected			
	Convalescent		Immune Adult	
	Number	Per Cent	Number	Per Cent
0 to 4	11	61.1	49	29.5
5 to 9	4	22.2	37	22.3
10 to 14	2	11.1	39	23.5
15 to 19	1	5.5	18	10.8
20 to 29	..	....	14	8.4
30 to 39	..	....	9	5.4
Totals	18	99.9	166	99.9

Table 4 gives the number of days after immunization that the measles rash developed among the group immunized with convalescent or adult serum.

COMMENT

In spite of the fact that statements are often found in the literature regarding the high degree of infectiousness of measles, there are only few reports on record which measure the exact degree of this contagiousness. Chapin,[10] from the city health department of Providence, R. I., reported that of 7,972 susceptible children under 15 years of age exposed to measles, 6,268, or 78.6 per cent, had the disease.

In the experiments here reported data were collected to determine the proportion of persons not immunized or having had an attack previously who when exposed to measles by familial contact developed the disease. Of 183 children between the ages of 6 months and 15 years thus exposed in Porto Rico, 149, or 81.4 per cent, developed measles.

Table 1 demonstrates that convalescent serum protected 84.2 per cent of the children immunized with it, while only 57.8 per cent of the number immunized with immune adult serum escaped the disease. Analysis of table 3, however, shows that the dose of serum played a major part in bringing about complete immunity in these children. Doses of 20 cc. or more of immune adult serums were apparently as efficacious as convalescent serum for the prevention of the disease.

As may be seen from table 2, more than 50 per cent of the children in each of the three groups were between 6 months and 5 years of age, and less than 15 per cent were over 10 years. It is shown that in the control group a larger percentage of the children over 10 years of age escaped the disease than in the younger groups. This may have been due to the greater opportunity for error in histories of previous attacks. This factor may have been responsible for the apparently higher protection in the older children in the group that received immune adult serum. Another factor that must not be ignored, however, is the fact that younger children often received smaller doses of serum, which may partly account for the smaller percentage protected.

Table 4 shows that of the immunized children who developed measles, 61.1 per cent of those receiving injections of convalescent serum and 29.5 per cent of those immunized with adult serums developed the measles rash from less than one to four days after immunization. This group of children presumably was well incubated previous to the administration of the serum. As a matter of fact, 2 children receiving injections of convalescent serum and 3 of the group immunized with adult serum had early symptoms of measles at the time the serum was injected.

Among more than 500 who received injections of serum, only 2 children showed reactions; they had slight fever, accompanied by an urticarial rash.

10. Chapin, C. V.: Am. J. Hyg. **5**:635, 1925.

It seems difficult to classify the patients in whom measles developed in our experiment by the severity of the disease. As a rule, measles is a comparatively mild illness in tropical countries when compared with the disease in a temperate climate. However, the attenuation of the disease as a result of the injection of convalescent or immune serums is a clearcut clinical feature easily observed. The modified or attenuated type of measles obtained in children immunized with convalescent or immune adult serum is usually characterized by a moderate rise in temperature, rarely ever reaching 39 C. (102.2 F.) and lasting only one or two days. The curious rash which accompanies the disease is scattered over the face and trunk and to a lesser extent over the extremities. The individual macules are about the size of a pinhead, and there are no erythematous patches, as observed in cases of unmodified measles. Conjunctivitis and coryza, when present, are mild. Fourteen of the 18 children receiving injections of convalescent serum who developed the disease had an attenuated case. Of 166 children who developed measles among the group immunized with adult serum, 68, or 41 per cent, had the condition in an attenuated form. None of the control group had this form. No complications developed among the immunized group, while in 4 of the nonimmunized children pneumonia developed, 2 of them dying. One of the children who died was severely malnourished and in poor health.

SUMMARY AND CONCLUSIONS

1. The prophylactic use of convalescent measles serum with good results has been reported by various investigators.

2. The use of immune adult serum in the prophylaxis of measles has also been encouraged, but little evidence is found in the literature regarding the true value of this agent.

3. Data are presented in this paper which give immune adult serum, in proper doses, a definite place in the prophylaxis of measles.

4. Of 120 children exposed to measles by familial contact and immunized with convalescent serum, 102, or 85 per cent, were completely protected. Fourteen of the 18 attacked in this group developed attenuated measles.

5. Of 132 children also exposed to the disease by familial contact and immunized with doses from 20 to 40 cc. of immune adult serum, 108, or 80.3 per cent, received complete protection and 20 of 26, or 76 per cent, of those attacked developed attenuated measles.

6. Doses of 10 and 15 cc. of adult serum gave complete protection in less than 50 per cent of the persons immunized, but usually resulted in an attenuated or mild form of the disease.

7. Of 183 untreated children (controls) living in the same houses with patients who had clinical cases and with treated children, only 34, or 18.6 per cent, failed to contract the disease.

8. Only 2 children had mild reactions among more than 500 who received treatment with serum.

9. It appears likely that a serious obstacle to the widespread use of convalescent serum will be the objection of some parents to the immunization of their children with serum obtained from strangers.

10. Immune adult serum is readily and universally available, and the technic for obtaining it from adults or children who have had the disease is simple and does not involve any risk.

11. Immune adult measles serum should be used with greater frequency for the protection of exposed children, especially for debilitated children, who probably die from the disease.

NITROGEN METABOLISM OF CHILDREN

WITH SPECIAL REFERENCE TO THE PROTEIN REQUIREMENT OF CHILDREN OF PRESCHOOL AGE *

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The object of this work was to determine whether children can maintain a positive nitrogen balance on less than 2.2 Gm. of protein per kilogram. In presenting the data I have recorded all of my experiments, including two that appeared to be failures but the analysis of which may also be of value.

Previous work on the protein metabolism of children, approached from the point of view of nitrogen balance, has been reported mostly by foreign writers. The experiments of Eric Muller [1] and Arnas Ruotsalainen [2] were carefully done from a technical standpoint but have been criticized by Holt and others, as have those of all workers in this field, on the ground that the subjects were undernourished or were children in institutions. In this report I have included observations on a few children living in their own homes and going to school, who were normal in all respects and who were receiving a normal diet.

HISTORICAL DATA

In 1907, Muller [1] made a metabolism study of thirty-two children in an orphan asylum. The work was done during the cool part of the year; from five to seven day preliminary periods were used for studying ordinary diet and six day periods for special diet. The author observed that the children investigated fell into various groups as to build, appetite, sleep and temperament, and that these groupings were important both in nitrogen balance and in energy studies. In the diets given, the proportion of average protein to other calories was 1:6.2, or 13.8 per cent protein to 86.2 per cent other calories. The children

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* From the Department of Pediatrics and Infectious Diseases, University Hospital.

1. Muller, Eric: Stoffwechselversuche an 32 Kindern im 3 bis 6 Lebensjahre mit besondere Berücksichtigung des Kraftwechsels auf Grund direkter calorimetrische Bestimmungen, Biochem. Ztschr. **5**:143, 1907.

2. Ruotsalainen, Arnas: Zur Kenntnis des Eiweissansatzes beim Kinde, Skandin. Arch. f. Physiol. **41**:33, 1921.

had an average nitrogen intake of 0.55 Gm. per kilogram per day, or 3.44 Gm. of protein. The total output of nitrogen was 3.18 Gm. Siegert,[3] in 1906, showed that the nursing growing child required 1 Gm. of protein per kilogram per day. He stated, however, that children from 3 to 6 years of age required from 3 to 4 Gm. of protein per kilogram.

Schlossman and Murschhauser,[4] in 1910, studied oxygen exchange and concluded that the difference between metabolism in children and adults is due to the need of additional growth material in the child. In 1912, Stargardter [5] studied three children for foods and protein requirement. He, however, changed the carbohydrate content from day to day, and thereby varied the total caloric intake.

In 1921, Ruotsalainen [2] ran an experiment similar to that of Stargardter, but with a total caloric value the same in different series of patients, varying only the type of food. To a series of patients with a sufficient basic protein intake, he added isodynamic quantities of fat, protein and carbohydate. He ran four series of ten days each. These subjects maintained a nitrogen balance on a protein intake of from 2 to 3 Gm. per kilogram per day. He further observed:

1. "If to a constant diet, protein, fat or carbohydrate be added, the nitrogen retention is greater when protein is added than when fat or carbohydrate is added.

2. "This is not only apparent but it continues if the protein content of the food is then reduced by half and an isodynamic quantity of sugar substituted. The nitrogen retention seems to be the expression of an actual protein addition." The absolute quantity of protein in the food must have an important relation to the "Eiweissansatz" of the growing child.

Holt and Fales,[6] in 1921, showed that children from 4 to 6 years of age excrete from 4 to 6 Gm. of nitrogen daily in the urine. This work was done on healthy, normal children. The figure is higher than that given by Muller and by Rubner.

In 1921, Holt and Fales,[7] in another study, which consisted of an analysis of the diets of 100 normal, healthy children, showed that the

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3. Siegert, E.: Der Nahrungsbedarf des Brustkindes im 1 Lebensquartal, München. med. Wchnschr. **53**:1980, 1906.

4. Schlossman, A., and Murschhauser, H.: Der Grundumsatz und Nahrungs bedarf des Säuglingsgemäss Untersuchungen des Gasstoffwechseln, Biochem. Ztschr. **26**:14, 1910.

5. Stargardter, J.: Beiträge zum Nahrungsbedarf und Eiweissbedarf des Kindes jenseits des Säuglingsalters, Arch. f. Kinderh. **57**:305, 1912.

6. Holt, L. E., and Fales, H. L.: Food Requirements of Children; I. Total Caloric Requirements, Am. J. Dis. Child. **21**:1 (Jan.) 1921.

7. Holt, L. E., and Fales, H. L.: Food Requirements of Children; II. Protein Requirement, Am. J. Dis. Child. **22**:371 (Oct.) 1921.

average protein intake of children under 6 years was 3 Gm. per kilogram and of those over 6 years, 2 Gm. per kilogram. In this series animal protein constituted 60 per cent of the total protein of the diet.

In glancing over the work of previous authors, it will be noted that most of them have placed the protein requirement at from 3 to 4 Gm. per kilogram. Ruotsalainen has shown in many of his experiments that children can maintain a nitrogen balance on as low a level as 2 Gm. of protein per kilogram. Therefore, there is a range of from 2 to 4 Gm. per kilogram, which is a rather wide variation for practical purposes. Furthermore, it is a known fact that many diabetic persons get no more than 2 Gm. per kilogram and are apparently able to maintain a nitrogen balance.

If one is to accept the results of the work of Newburg and others of his school which show that a high protein diet is injurious, it would seem important to reduce the protein intake to as low an amount as would be consistent with the maintenance of a positive nitrogen balance. There is, however, no uniformity of belief on this question.

It was my purpose to determine whether the children in this group would be able to maintain a balance with less than 3 or 4 Gm. per kilogram, the amounts recommended by Holt and others. I, therefore, commenced my work with the arbitrary requirement of 1 Gm. per pound or 2.2 Gm. per kilogram.

COLLECTION OF SPECIMENS

Twenty-four hour specimens were first collected without altering the diets. By so doing, I thought that I might unearth difficulties that were not apparent at the onset. By persistent effort the teacher and the mother were able to train the child to collect specimens properly. All vessels were supplied charged with the necessary preservative to prevent decomposition (1 cc. of hydrochloric acid). The parent was instructed to keep the specimen in a cool place until delivered at the laboratory.

In collecting the fecal specimens, it was found that in transferring the fecal material from the vessel to the container which was sent to the laboratory, a certain amount was lost. This was prevented by covering the bottom of the vessel with a waxed paper napkin, the napkin being lifted out with its contents and transferred to the laboratory container.

CALORIC REQUIREMENT

It was a question whether to accept 80 or 100 calories per kilogram as the daily caloric requirement. The Pirquet system,[8] in which the

8. Pirquet, Clemens: An Outline of the Pirquet System of Nutrition, Philadelphia, W. B. Saunders Company, 1922.

arbitrary unit of the nem is used, was chosen as the most suitable for the purpose. The formula is as follows:

(Sitting height in centimeters)$^2 \times 7/10 \times 2/3$ = calories required per twenty-four hours for the healthy child with normal activity.

In this formula the square of the sitting height in centimeters represents the nutrition surface of the body. The maximum that a child can digest is 1 nem per square centimeter. (A "nem" represents the nutritional value of 1 Gm. of milk.) The minimum that he requires if he stays in bed without moving is 3/10 nem or 3 "decinems" per square centimeter. Though a normal healthy boy or girl would sit still in school for some hours, he is likely to be active during the rest of the day. He is given, therefore, 3 decinems more than the minimum requirement in order to maintain his weight, that is, 6 decinems per day. It is desirable, however, not only to maintain his weight, but to provide for growth and gain in fat and muscle, so he is given 1 decinem more or 7 decinems per square centimeter, an optimum requirement. This requirement in nems is converted into calories by multiplying by 2/3.

DIET

The only requirements set forth in the diet were that the calories should be fixed for twenty-four hours, and that the subject should have 1 Gm. of protein per pound, two thirds of which should be animal protein. The mothers were instructed by the dietitian in the art of so distributing the required fat through the diet that it was not distasteful.

The mother was given the diet list and a scale weighing in grams. She was taught how to weigh the diets called for and was supervised until I was sure that her figures could be relied on. She was also carefully instructed in the principles of dietetics.

The diet schedules were prepared a week ahead, a different menu for each day. Each diet sheet was accompanied by weighing sheets which the mother filled out as instructed. The food was weighed before eating, on the dish on which it was served. After eating, the dish was again weighed and the amount consumed computed.

CHEMICAL METHODS

Nitrogen determinations were made daily on the urine and feces by the standard Kjehldal method. The stool was placed in a drying oven at 100 C. and dried to constant weight.

CASE 1.—P. S., an American girl, aged 5 years, at Merrill Palmer School, weighed 16.53 Kg. (36.36 pounds); a sitting height was 57.85 cm., the standing height, 102.1 cm.

The results of the physical examination, including complete tests on the blood, urine, etc., were essentially negative. She was one of the most perfect physical specimens in the school.

With the Pirquet formula, the caloric requirement for the child was 43 per pound or about 94 per kilogram ($7/10 \times 57.85$ cm.$^2 \times \frac{2}{3} = 1{,}561$ calories per twenty-four hours). The figure is somewhat higher than

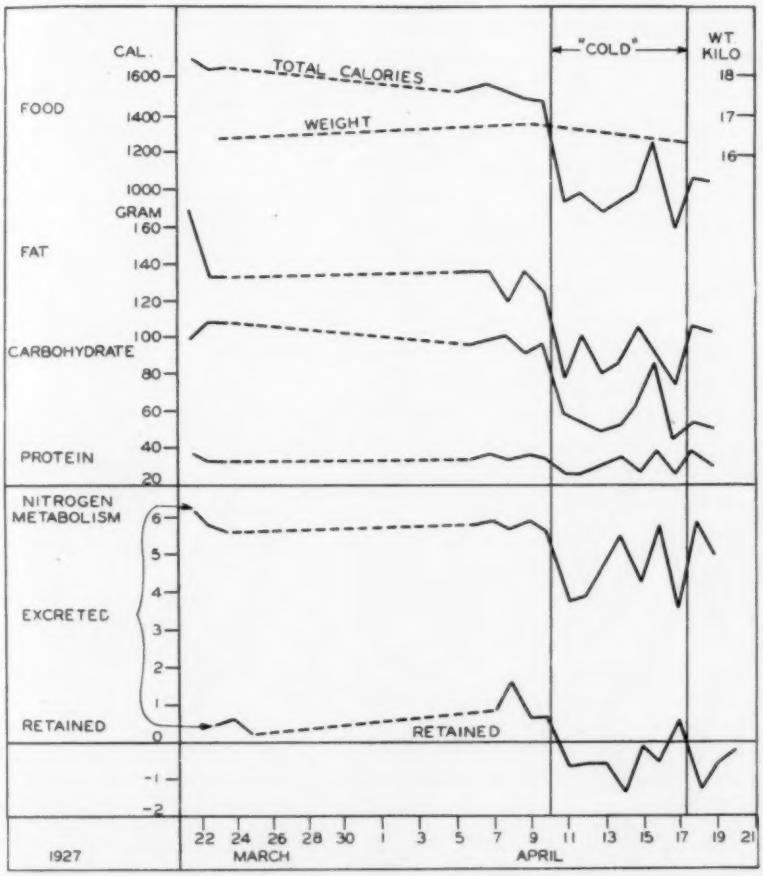

Chart 1 (case 1).—Food intake, weight and nitrogen balance over thirty day period of a normal school child with infection of the upper respiratory tract, which occurred on April 10.

that obtained from the Holt and Fales tables, yet it is within the accepted normal range.

By reference to chart 1 it will be seen that this child remained in positive nitrogen balance from March 22 to April 10. At this time she went into a negative nitrogen balance. It is of interest to note

that she put out about from 5 to 6 Gm. of nitrogen per twenty-four hours whether she was in positive or in negative balance. No voluntary changes in diet had been made that would put the subject into a negative balance. About April 10 she developed an upper respiratory infection and refused from 30 to 40 per cent of her diet. The dietary omissions at this time were most marked in fat and carbohydrate. I believe that this child would have refused a great deal more food had not the mother insisted on her eating. Children with upper respiratory infections frequently lose their appetite. This was a common observation during the influenza epidemic that was prevalent at this time.

The development of the infection in this child introduced a factor that I was hoping to avoid. The case was set aside with the intention of not including it in this report. Its analysis, however, may yield information of some value.

As shown by Ruotsalainen, protein can be materially reduced and an isodynamic quantity of carbohydrate added in its place and the subject remain in positive balance.

In the records of case 1, I observed that during the infection the child took less than the required amount of protein and soon went into a negative nitrogen balance. Now following Ruotsalainen's idea, a positive balance could be produced by forcing the eating of carbohydrate and fat. The child, however, was already taking more than she would of her own free will. In order to maintain the nitrogen balance on a minimum protein intake, the diet becomes so bulky that it may be difficult for a sick person to take.

CASE 2.—B. S., an American girl, aged 3½ years, at Merrill Palmer School, weighed 14.9 Kg.; the sitting height was 41.2 cm., the standing height, 88.5 cm. The results of the physical examination, including complete tests on the blood, urine, etc., were essentially negative.

The Pirquet formula showed that the caloric requirement was 1,330 per twenty-four hours, about 32 calories per pound (92 calories per kilogram). The diet was made up of 1 Gm. of protein per pound (2.2 Gm. per kilogram) and sufficient fat and carbohydrate to make up the calories.

In chart 2 it will be seen that this child remained in positive nitrogen balance and excreted from 2.5 to 3 Gm. of nitrogen per twenty-four hours. From July 21 to August 12 no change was made in the diet. On August 12, the protein intake was reduced to 0.66 Gm. per pound, or 1.46 Gm. per kilogram. If, according to Ruotsalainen, one should replace the protein with an isodynamic quantity of carbohydrate, the child would still remain in positive nitrogen balance. This necessitates a knowledge of the isodynamic protein equivalent of carbohydrate.

The figure must depend on the degree of perfection of the metabolism in the child. It seems reasonable to assume that in the presence of perfect metabolism it would take more than 1 Gm. of carbohydrate to balance every gram of protein withdrawn. The carbohydrate was raised approximately 13 Gm. and the fat 5 Gm. The rise in the fat was incidental, being a more convenient way to obtain the exact number of calories. Ruotsalainen showed that fat also has an isodynamic protein value, perhaps not quite as great as that of carbohydrate.

With this change in diet, there seemed to be a tendency for the child to go into a negative nitrogen balance; adjustment, however, soon

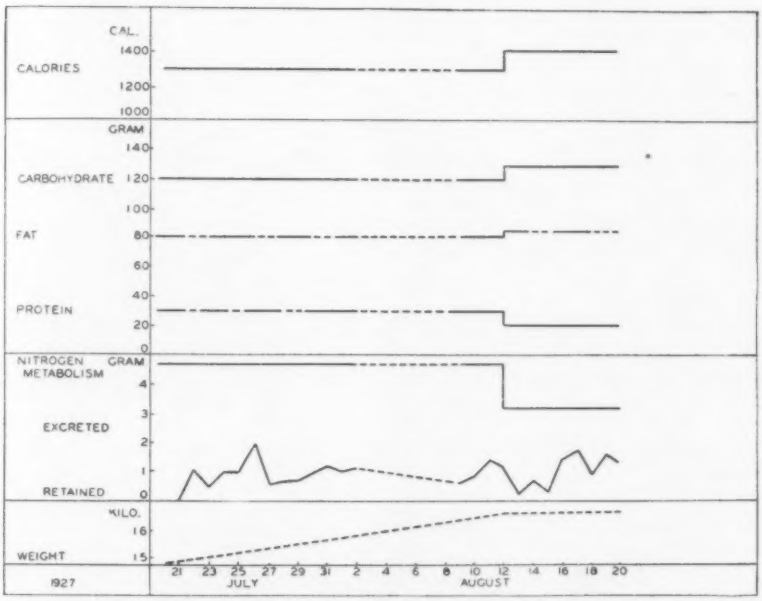

Chart 2 (case 2).—Food intake, weight and nitrogen balance over thirty day period of a normal school child in whom the positive nitrogen balance was maintained with 1.46 Gm. of protein per kilogram.

took place, and she maintained a definite positive balance. These observations show that nitrogen balance can be maintained on less than 1 Gm. of protein per pound, or 2.2 Gm. per kilogram (0.66 Gm. of protein per pound, or 1.46 Gm. per kilogram). It would even seem that a balance could have been maintained on a somewhat smaller amount of protein.

The first ten days the child was on this diet she gained 2½ pounds (1.1 Kg.); the second ten days she gained only ½ pound (0.2 Kg.); the third ten days she made no gain. The only explanation for the sudden gain the first ten days is that the diet called for more food than

she ordinarily took. After a week she adjusted herself to the new amount. Up to August 12 she gained 3 pounds (1.4 Kg.), thereby increasing the protein requirement. If the new protein requirement is calculated according to her increased weight, she was really not getting as much as 0.66 Gm. of protein per pound (1.46 Gm. per kilogram), but only 0.58 Gm. per pound (1.16 Gm. per kilogram).

CASE 3.—H. S., an American boy, in Merrill Palmer school, weighed 39⅜ pounds (17.9 Kg.); his sitting height was 24 inches (60 cm.), the standing height, 43.75 inches (109.3 cm.).

The results of the physical examination of this child, including tests on the blood and urine, were essentially negative.

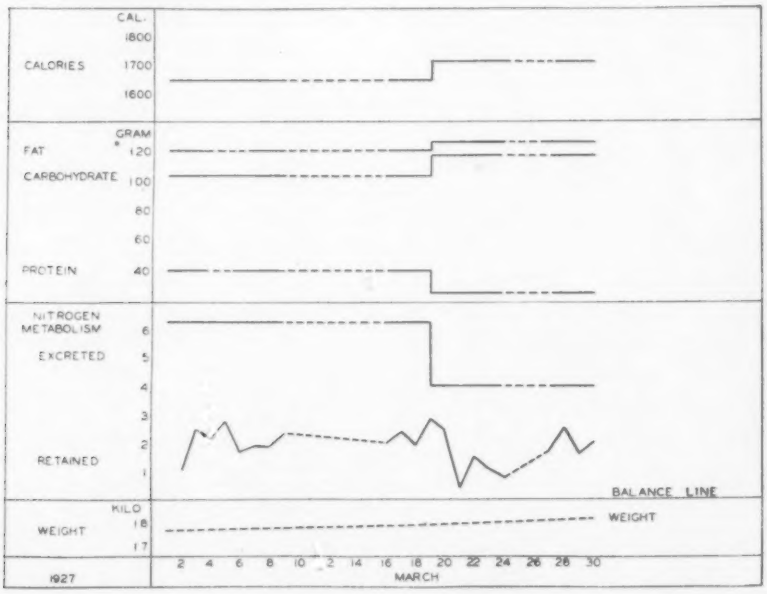

Chart 3 (case 3).—Food intake, weight and nitrogen balance over thirty day period of a normal school child in whom the positive nitrogen balance was maintained with 1.46 Gm. of protein per kilogram.

According to the Pirquet formula, the required calories were 1,640 per twenty-four hours. I began my observations by giving 1 Gm. of protein per pound of body weight, or 2.2 Gm. per kilogram. The total diet consisted of 39.6 Gm. of protein, 105 Gm. of carbohydrate and 120 Gm. of fat.

As will be seen in chart 3, from March 2 to 9 the child was on this carefully weighed diet. During this period, he was in a definitely positive nitrogen balance and excreted from 4 to 5 Gm. of nitrogen per twenty-four hours. From March 9 to 16, the diet was not weighed. By a system of relative measuring, I endeavored to give the same amount

of food. Observations on the urine and stools were not made during this period. On March 16, weighing the diet and daily nitrogen determinations on the stools and urine were resumed. From March 16 to 19 the child was in a definitely positive nitrogen balance and was putting out about 14 Gm. of nitrogen per day. On March 19, the protein intake was lowered 14 Gm. to approximately 0.78 Gm. per kilogram. To maintain a positive nitrogen balance on this small intake of protein 51 calories were added to the previous energy intake (carbohydrate, 15 Gm.; fat, 5 Gm.). While the child was on this diet, he at one point came close to a negative nitrogen balance. From March 24 to 27 is another period when the diet was not weighed and the urine and feces were not analyzed. From March 27 to 30, weighing and analysis were resumed. Again it is noted, as in the previous case, that the child adjusted himself to a change in diet and maintained the usual nitrogen balance.

This child was slightly underweight when our observations began. During the period of observation, he gained 1 pound (0.5 Kg.). The investigation shows that a child can maintain a nitrogen balance on about 0.66 Gm. of protein per pound. On March 16, he weighed 39.8 pounds (18 Kg.). On March 19 and at the end of the experiment, he weighed 40.2 pounds (18.2 Kg.). During the first period of observation, he was given 39.2 Gm. of protein in twenty-four hours, 1 Gm. per pound of body weight. During the second period (March 19), when his weight was 40.2 pounds, the protein intake was reduced to 25 Gm. in twenty-four hours (0.6 Gm. per pound, 1.46 Gm. per kilogram).

CASE 4.—R. H., aged 12 years, was a patient in the pediatric service of the University of Michigan Hospital, suffering from a mild form of diabetes mellitus. His weight at the beginning of the observations was 83 pounds (37.7 Kg.); the standing height was 138.7 cm., the sitting height, 57 cm. This boy had always been in good health and was still considered to be in good health at the time of admittance. During a routine physical examination, sugar was discovered in the urine. Questioning disclosed that he had a polyuria, increased thirst and a rather ravenous appetite. He was sent in to the University of Michigan Hospital for study.

Physical examination on entrance revealed nothing of importance. In fact, he had every appearance of being a perfectly normal, well nourished boy. The blood sugar was 0.210 per cent; the sugar in the urine was ++, and the test for acetone and diacetic acid was positive.

He was given a diet of 1,500 calories (40 Gm. of carbohydrate, 60 Gm. of protein, 123 Gm. of fat) and 5 units of insulin three times a day. Almost at once he became sugar-free, and the blood sugar returned to normal. Within a few days, he again showed sugar and continued to do so in spite of increasing doses of insulin. He was stealing food. It became necessary to put him to bed in order to control his diet. On this rigid régime, he became sugar-free, and the use of

insulin became unnecessary. His diet was gradually increased to 1,682 calories (60.5 Gm. of protein, 45 Gm. of carbohydrate, 140 Gm. of fat). He still remained free from sugar, acetone and diacetic acid. His blood sugar varied within the normal range, from 0.09 to 0.115.

At this point I began my observations. It will be seen from chart 4 that the patient remained on the diet of 1,682 calories. His weight was 83 pounds (37.7 Kg.). At the end of the observation period it was also 83 pounds. From May 5 to 16, he had a negative nitrogen balance, excreting from 8 to 10 Gm. of nitrogen in twenty-four hours. From May 17 to 18 he went into a positive nitrogen balance. An investigation disclosed that on the night of May 16 he again broke the diet. The experiment was terminated, and unfortunately he was shortly afterward discharged.

The patient in case 2 (chart 2) maintained a positive nitrogen balance on 0.58 Gm. of protein per pound, or 1.27 Gm. per kilogram, and the one in case 3 (chart 3) maintained a positive nitrogen balance on 0.6 Gm. per pound, or 1.32 Gm. per kilogram, while the patient in case 4 went into a negative nitrogen balance on 0.75 Gm. per pound, or 1.65 Gm. per kilogram. Why this wide difference? One might think it due to the fact that the patient was not getting sufficient calories. The patient in case 2 was getting 43 calories per pound (96 calories per kilogram); the one in case 3, 42 calories per pound (92 calories per kilogram). The patient in case 4, on the other hand, was getting only about 20 calories per pound (44 calories per kilogram). If the caloric requirement is figured according to the Pirquet formula, it being remembered that the patient was confined to bed, one finds that it was slightly more than adequate. This calculation, of course, is not exact. The factor "strictly confined to bed" will vary a great deal with different patients, and accordingly the amount of energy consumed will vary greatly. Some children become restless when confined to bed and thus consume more energy than those who are more tranquil. It is possible that the patient in case 4 was not getting an adequate number of calories. Furthermore, it should be remembered that this subject, because of his diabetes, had not the perfect metabolism possessed by the two normal children (cases 2 and 3). I think that I am justified in this conclusion even though at this time he remained sugar-free. His metabolism was still impaired. Doubtless he did not get the full isodynamic protein equivalent from his carbohydrate or fat. If this hypothesis is true, it becomes more and more apparent that the patient was underfed. A certain number of extra calories, representing the various foods, should be allowed for waste in any case in which the metabolism is not 100 per cent perfect. Why figure calories to fractions when one has no conception of the degree of perfection of the patient's metabolism?

This recalls Dr. Cowie's strong plea [9] for diabetic persons: "Give them enough food so that they are satisfied and don't have to steal—covering their excess load with insulin." A similar plea came from J. P. Peters,[10] especially for nephritic patients. He considered patients with other metabolic diseases as well. In a recent article, Du Bois [11] made the following statement: "Unless I am greatly mistaken, we are going to pay more attention in the future to the dangers of partial protein starvation in chronic diseases."

When one recalls that the physicians in charge of this patient considered that "the patient had sufficient food for being confined in bed,"

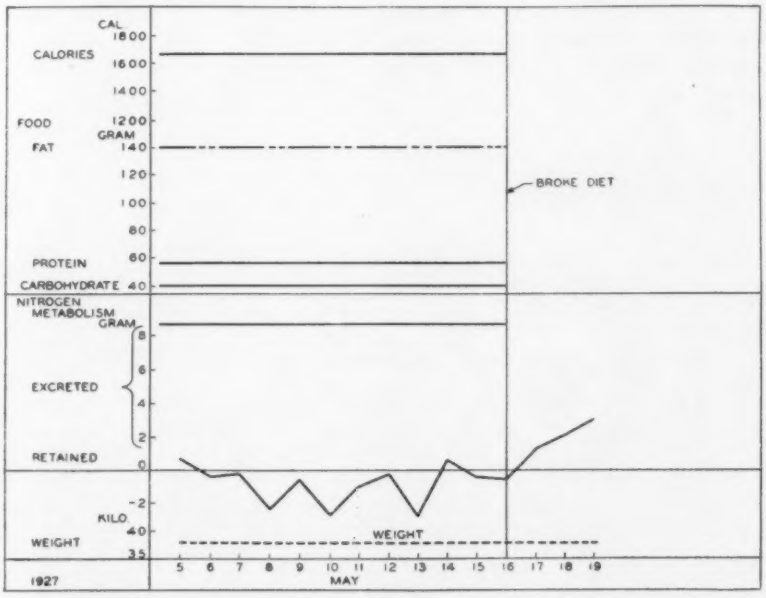

Chart 4 (case 4).—Food intake, weight and nitrogen balance over ten day period of a mild diabetic child who was in negative nitrogen balance with 1.65 Gm. of protein per kilogram.

the significance of this becomes obvious. Chart 4 illustrates the point very well, the patient being in negative nitrogen balance throughout.

9. Cowie, D. M., and Parsons, J. P.: Clinical Observations on the Use of Insulin in the Treatment of Diabetes in Adults and Children with Particular Reference to the State of Hyperinsulinemia; A Consideration of Insulin and Renal Glycosuria, Tr. Am. Pediat. Soc. **35**:217, 1923.

10. Peters, J. P.: The Principles of Diet Control in Nephritis with Especial Reference to Protein and Salt Restriction, J. Am. Dietet. A. **2**:137, 1926.

11. Du Bois, E. F.: The Control of Protein in the Diet, J. Am. Dietet. A. **4**: 53, 1928.

Case 5.—B. E., aged 4 years, weighed 37 pounds (16.8 Kg.); the standing height was 101 cm., the sitting height, 52.2 cm. The patient entered the University Hospital on Oct. 1, 1925. He had been considered well until about one month before entrance. At this time the mother noted marked thirst, frequency of urination, craving for sweets and loss of weight.

On physical examination, little was found. While he had lost weight, he was still within the normal range. His skin was somewhat dry; the hair had lost its luster. His blood sugar was 0.25 per cent; the urine showed sugar +++ and a strongly positive reaction to acetone and diacetic acid.

This patient was placed on 1,500 calories: 45 Gm. of protein, 49 Gm. of carbohydrate, 125 Gm. of fat and 4 units of insulin three times a day. His urine soon became sugar-free, and his blood sugar returned to normal; the dosage of insulin was reduced to 2 units twice a day. In the spring his improvement was so marked that insulin was entirely withdrawn, and the patient was discharged.

He had been home but a few weeks when, on April 6, 1926, he returned with his urine showing ++++ sugar and considerable amounts of acetone and diacetic

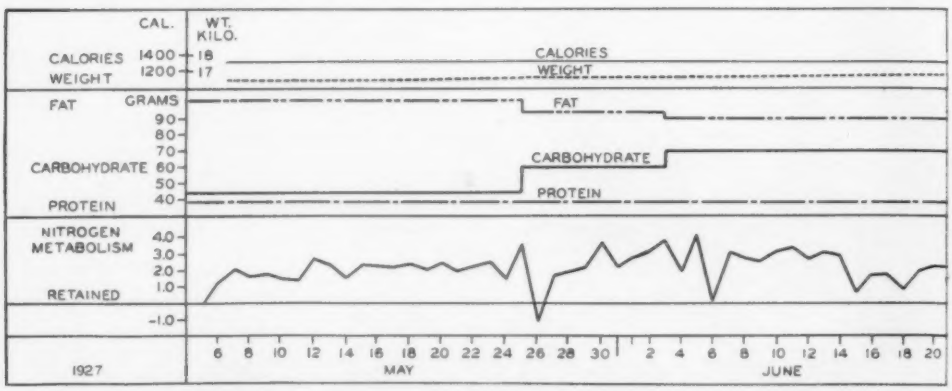

Chart 5 (case 5).—Food intake, weight and nitrogen balance over forty-five day period of a diabetic child in whom the protein intake was kept constant with variations in the carbohydrate intake.

acid. His blood sugar was 0.35 per cent, much higher than at any previous time. The diet was reduced to 1,263 calories (38 Gm. of protein, 45 Gm. of carbohydrate, 103 Gm. of fat). Four units of insulin three times a day were necessary. Two weeks later, I was able to reduce the insulin to 2 units twice daily. This brings the progress of the case up to May 5, when my observations began. There had been a period of two weeks during which the patient's urine was sugar-free and his blood sugar normal (0.115 per cent).

According to the Pirquet formula, this patient required 1,272 calories, practically the amount called for in the diet he had been placed on. Referring to chart 5, it will be seen that from May 5 to 25 he remained on this diet, was in definite positive nitrogen balance and was excreting from 3 to 4 Gm. of nitrogen per twenty-four hours.

Chart 6 is a composite of chart 5. It is shown that the subject had a constant caloric intake and a constant protein intake. Throughout

the period he was excreting from 2 to 6 Gm. of nitrogen per day. On May 26, when the carbohydrate intake was increased, the nitrogen retention increased. The carbohydrates were further increased on June 3, and again the nitrogen retention increased.

This effect would have been expected if the protein intake had been made greater and the other constituents of the diet left the same. The increased retention of nitrogen with the constant nitrogen intake, caused by increasing the carbohydrate, is difficult to explain. The carbohydrate must either facilitate a more perfect metabolism of the protein, thus making more nitrogen available, must aid in the process of storing

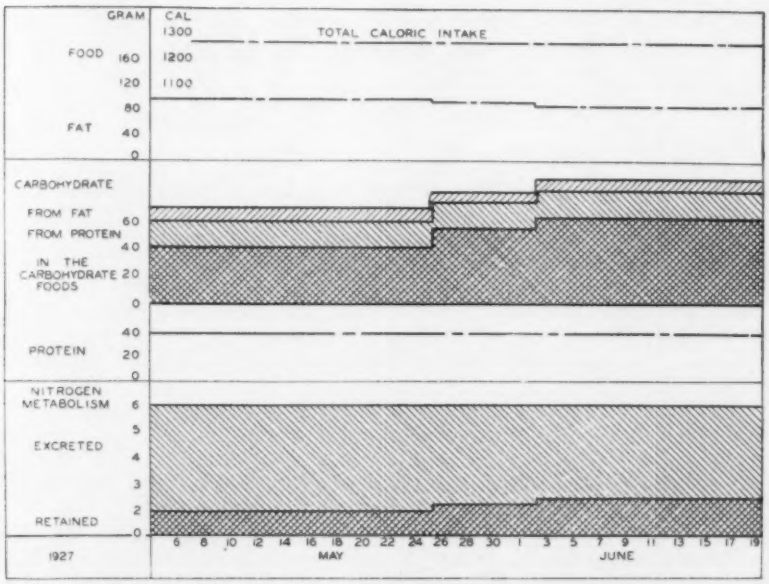

Chart 6.—Composite of chart 5, showing an increased nitrogen retention with an increase of the carbohydrate intake.

nitrogen or must interfere with the excretion of nitrogen. In case 2 the decrease in the protein intake alone would have produced a definitely lowered nitrogen retention, but with the carbohydrate increased the retention was maintained at the same, if not at a higher level. In chart 3 is shown a similar situation. The carbohydrates seem to exert an isodynamic effect on the protein metabolism.

Chart 7 deals with the same case, but begins at a later period and runs much longer. The general condition of the patient throughout this entire experiment was excellent.

The daily temperature variations are shown at the bottom of this chart. The next curve above shows the daily nitrogen retention, and

immediately above this the nitrogen intake is marked off in blocks. Above this is the actual height curve drawn in a solid line. The fine dotted line below and almost paralleling it is the Baldwin theoretical height curve. It is remarkable that the actual height curve should so perfectly parallel the theoretical curve. It would at least seem to show that the patient was developing normally. The irregular curve above the height curves records the daily fluctuations in weight. Through it in dots and dashes is drawn an average weight curve. The fine dotted line below the weight curves represents the theoretical weight as determined by Baldwin.[12] The actual weight curve closely parallels the theoretical curve. These curves are also consistent with Talbot's [13] work on metabolism in which he shows that a child grows in length at one time of the year and puts on weight at another time.

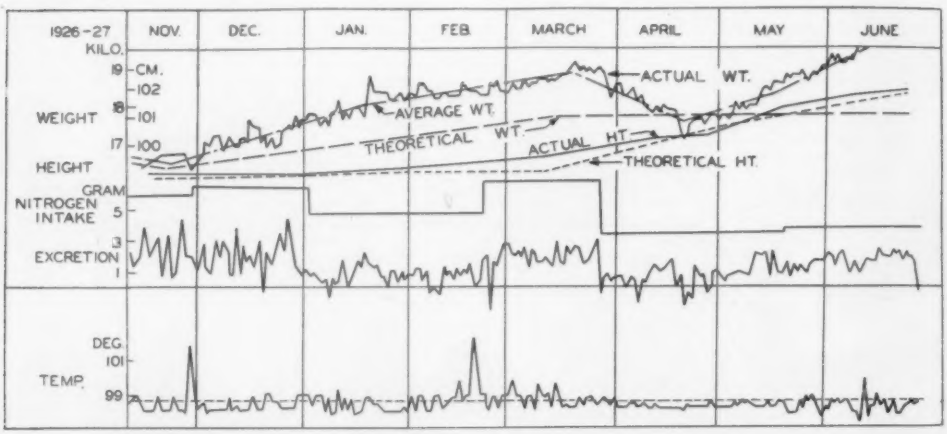

Chart 7.—Further study of case 5, showing the weight, height, temperature and nitrogen balance over a period of seven months. The carbohydrate intake was kept constant with variations in the protein intake. The positive nitrogen balance was maintained with only 1.18 Gm. of protein per kilogram.

The wide fluctuations in the nitrogen retention curve show the value and necessity of daily rather than of five day period determinations.

The temperatures in case 5 are all rectal. Only on three occasions did the patient run a high temperature for a fraction of a day.

Chart 8 is a composite of chart 7. The lowest curve shows the nonprotein nitrogen of the blood, which at the outside varies only about 8 mg. Under nitrogen retained, one finds the composite curve of the

12. Baldwin, Bird T.: Physical Growth of Children from Birth to Maturity, University of Iowa Studies, Studies in Child Welfare, vol. 1, no. 1, 1921, p. 60.

13. Talbot, F. B.: The Internal Secretory System and Metabolism in Infancy and Childhood. Clinical Pediatrics, New York, D. Appleton & Company, 1928, vol. 13.

daily nitrogen retention variations seen in chart 7. As in the previous composite chart, I have again averaged the daily nitrogen retentions for each dietary period. Throughout the eight months the patient excreted from 2 to 4 Gm. of nitrogen per twenty-four hours.

In a dot and dash line, I have indicated the protein food intake. This does not entirely parallel the nitrogen retention line. Above this is seen first the block representing the carbohydrate intake, practically a straight line. The next block represents the carbohydrate available from fat, and the block above this that available from protein. The sum of the three blocks gives the total available carbohydrate in the

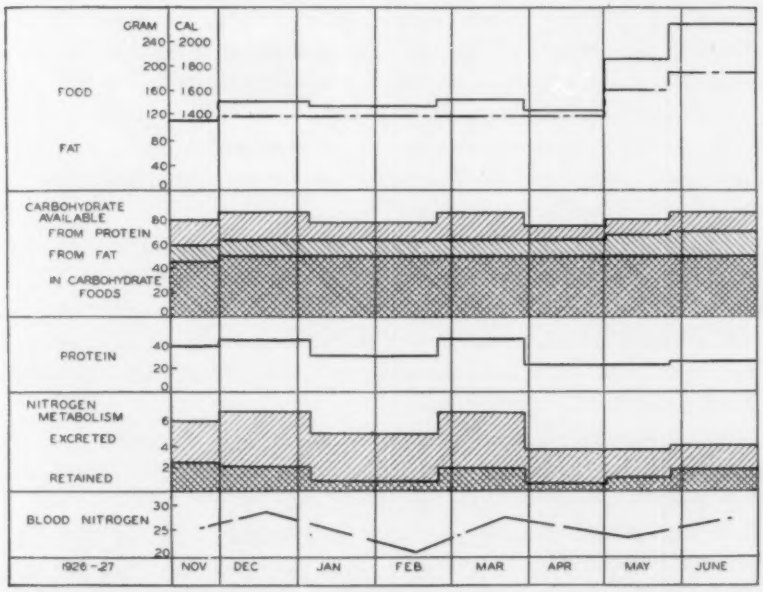

Chart 8.—Composite of chart 7; the line representing the total available carbohydrate parallels the nitrogen retention curve almost exactly.

foods. It is of great interest to note that the line indicated by the total available carbohydrate is the only one on the chart that parallels the nitrogen retention curve almost exactly.

It will be observed that during the month of April and the greater part of May the patient was ingesting only 20 Gm. of protein per day, 0.54 Gm. per pound or 1.18 Gm. per kilogram, was in positive nitrogen balance and was even storing nitrogen. During January and February, the patient was ingesting about 30 Gm. of protein per day. He remained in a positive nitrogen balance but did not show evidence of storing nitrogen as he did in April, May and June. To store nitrogen on a minimum protein intake apparently requires added energy.

COMMENT

In 1920, H. C. Sherman [14] compiled data from 109 experiments made by many observers. From this work he showed that a positive nitrogen balance was maintained on 0.6 Gm. of protein per kilogram of body weight, 0.27 Gm. per pound. For the average adult this would mean about 40 Gm. per twenty-four hours. This seems an unusually low protein intake. It should be remembered, however, that his subjects were all adults, who require no extra protein for growth and development.

In determining the absolute minimum daily protein requirement necessary to maintain a positive nitrogen balance, daily nitrogen determinations should be made over considerable periods of time. Much depends on whether there is any protein storage in the patient at the beginning of the experiment. Peters,[10] working in Rubner's laboratory, and Murlin,[15] working in Lusk's laboratory, have shown independently that the avidity with which the adult organism retains nitrogen is greater, the greater the previous losses of protein from the body have been.

An average infant, aged 1 year, weighing 21 pounds (9.5 Kg.), who is taking about 40 ounces or 1,200 cc. of milk daily, an amount equivalent to 42 Gm. of protein, is getting 2 Gm. of protein per pound or 4.4 Gm. per kilogram. The soft diets for infants on the ward carry about from 35 to 42 Gm. of protein per twenty-four hours, an average of from 2 to 2.22 Gm. per pound.

Comparing these diets with those of children in the same age group in the outpatient service, I find that the outpatient child has a much higher protein intake.

Sherman placed the protein intake of breast-fed infants at about 9 per cent of the total calories. The same infant when bottle-fed doubtless will take considerably more protein. Hoobler [17] has shown experimentally that protein in the amount of 10 per cent of the total calories is as high a proportion of protein as an infant is likely to utilize, consistent with the highest efficiency in the growth of body tissue. If, then, the full grown man and the child at the time of most rapid growth require 10 per cent of their total calories in the form of pro-

14. Sherman, H. C.: Protein Requirement of Maintenance in Man and the Nutritive Efficiency of Bread Protein, J. Biol. Chem. **41**:97, 1920.

15. Murlin: The Nutritive Value of Gelatin: II. No. 2. The Significance of Glyocoll and Carbohydrate in Sparing the Body's Proteid.

16. Footnote 16 was deleted by the author.

17. Hoobler, B. R.: The Protein Need of Infants, Am. J. Dis. Child. **10**:153 (Sept.) 1915.

tein, it would seem probable that this proportion is sufficient for any intermediate age if the protein is the right kind.

The children objected to the higher amount of fat and lower amount of meat than they were accustomed to. Children in general, and especially infants, consume relatively high amounts of protein.

Newburgh [18] and Squier and Newburgh [19] have presented a great deal of evidence of a harmful action of high protein diets on the kidneys and arteries of rabbits. Polvogt, McCollum and Simmonds [20] and Evans and Risley [21] reported lesions in the kidneys of young rats on high protein diet. Osborne and Mendel [22] reported hypertrophy but no degenerative changes of the kidneys of white rats fed on high protein diets without carbohydrates. MacLean, Smith and Urquhart [23] placed rabbits on a high protein diet with fresh vegetables. No deleterious effect was produced on the kidneys. Addis, MacKay and MacKay [24] recorded similar results.

With the foregoing experimental work in mind, it is difficult to understand how Eskimos thrive on the diet described by Stefansson. Certain tribes live almost exclusively on meat and fish with no vegetables.

Opinions on this point differ widely. More work is needed to settle the question of nitrogen storage and whether a negative nitrogen balance always means tissue destruction. In chart 7 it will be seen that the child went into a negative nitrogen balance during the time she had an infection of the upper respiratory tract. During the acute phase of such an infection, a patient is more or less toxic. Considerable water may be bound in the tissues. Protein, unlike carbohydrate and fat, requires ample free water to expedite its complete metabolism. This not being available, the required protein cannot be properly utilized, so that previously stored nitrogen may be spilled. May not

18. Newburgh, L. H.: The Production of Bright's Disease by Feeding Protein Diets, Arch. Int. Med. **24**:359 (Oct.) 1919.

19. Squier, T. L., and Newburgh, L. H.: Renal Irritation in Man from High Protein Diet, Arch. Int. Med. **28**:1 (July) 1921.

20. Polvogt, L. M.; McCollum, E. V., and Simmonds, N.: Production of Kidney Lesions in Rats by Diets Defective Only in that They Contain Excessive Amounts of Protein, Bull. Johns Hopkins Hosp. **34**:168, 1923.

21. Evans, N., and Risley, E. H.: High Protein Ration as Cause of Nephritis, California & West. Med. **23**:437, 1925.

22. Osborne, T. B., and Mendel, L. F.: Nutrition and Growth on Diets Highly Deficient or Entirely Lacking in Preformed Carbohydrates, Am. J. Physiol. **68**: 167, 1924.

23. MacLean, H.; Smith, J. F., and Urquhart, A. L.: Effect of High Protein Diet on Renal Function, Brit. J. Exper. Path. **7**:360, 1926.

24. Addis, T.; MacKay, E. M., and MacKay, L. L.: Effect on Kidney of Long Continued Administration of Diets Containing Excess of Certain Food Elements: Excess of Protein and Cystine, J. Biol. Chem. **71**:139, 1926.

a negative nitrogen balance be a protective mechanism, as refusal of food by a patient may be a protective mechanism? I have called attention to the anorexia of influenza, when the patient often takes only water. There is probably always a negative nitrogen balance during this period. Should concentrated protein be given at such a time by ingestion and by the intravenous route? The patient needs "free water," and a high protein diet would probably bind the water. The situation is different from that in a chronic illness in which the patient becomes accustomed to functioning on less free water.

In this report I have shown that a child can maintain nitrogen balance on from 0.5 to 0.66 Gm. of protein per pound. These figures are different from those previously given by Holt and Fales. Although in ordinary life this difference in figures has little significance, certainly during war, famine and similar situations it may be of scientific importance to know that the body can function normally on such small amounts of protein. Whether or not it is best for a normal person to be on a high or low protein diet is an important question.

Matthews, in his definition of a food, includes oxygen, salt and water as true foods, being necessary chemicals required to complete metabolism. The amount of oxygen on which the body can function is not fixed. People at high altitudes have as good health as those at sea level. If a very young or old person, however, is suddenly brought from a very high to a low altitude, serious disturbances may result and prove fatal.

A person can apparently function with a relatively small amount of water and yet can take large amounts of water without impairment. I am familiar, however, with cases in which infants are given repeated infusions, which result in little more than water intoxication.

Again, one is familiar with the man who travels widely, necessitating frequent changes from high protein to high fat diets. If he is not careful in making his adjustment disturbances result, but if the change is made gradually he has no difficulty. Members of Stefansson's [25] expeditions in the north have gone on a comparatively high protein diet for a number of years without any apparent difficulty.

Looking on protein and particularly its metabolites in the same light as other chemicals such as oxygen and water, it seems reasonable to expect a person to be able to adjust himself to a high or a low protein diet and still maintain an efficient metabolism. Conclusions should no more be drawn from the results of such a sudden change in diet than they would if an herbivorous animal were suddenly placed on a

25. Stefansson, V.: The Stefansson-Anderson Arctic Expedition of the American Museum: Perliminary Ethnological Report, Anthropological Papers of the American Museum of Natural History **14**:47, 1919.

carnivorous diet. Becoming accustomed to a high fat or to a high or low protein diet is no doubt as much a problem of acclimatization as is the adjustment to a high or a low oxygen tension.

CONCLUSIONS

1. The lower limit of the amount of protein on which a child can function efficiently depends on the degree of perfection of his metabolism.

2. Evidence is presented to show that a healthy child of the age group from 4 to 8 years can maintain a positive nitrogen balance on 0.5 Gm. per pound, or 1.1 Gm. per kilogram.

3. Evidence is presented to show that with insulin a diabetic child can maintain a nitrogen balance and make normal development on 1 Gm. of protein per pound, or 2.2 Gm. per kilogram.

4. To maintain the nitrogen balance on a minimum protein intake, it is necessary to replace the withdrawn protein by an isodynamic equivalent of carbohydrate or fat, as was demonstrated by Ruotsalainen.

5. Evidence is presented to show that in acute infections when children refuse a great deal of food they go into a negative nitrogen balance.

ASTHMA IN CHILDREN

X. THE RÔLE OF KETOGENIC AND LOW CARBOHYDRATE DIETS IN THE TREATMENT OF A SELECTED GROUP OF PATIENTS *

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AND
A. H. FINEMAN, M.D.
NEW YORK

With the introduction of the protein skin tests in the past decade considerable progress has been made in the study and care of children suffering from bronchial asthma. A practical method of classification of asthma along etiologic lines is now possible and is of extreme value since it leads directly to rational therapy. As a result of modern therapy, the percentage of children definitely improved or relieved from asthma ranges widely, according to the reports in the literature, from 40 to as high as 90. Thus, between 10 and 60 per cent of the patients who have received accepted standard modern investigation and treatment continue to have asthma. Within this class of unimproved patients there exists, in our experience, a subgroup of children in whom the asthma remains severely chronic from the point of view of intensity, frequency and long duration of the attacks. In these cases little can be done to give relief until nature itself restores the "physicochemical balance." In a recent communication,[1] it was concluded that until newer methods are advanced that will successfully control the asthma of this group of children or free them from it, a "home" prepared to accommodate children with chronic asthma of the refractory type for at least six months is a humane and economic necessity, as well as a therapeutic measure of definite value.

In an attempt to decrease the number of children recommended for treatment by a change of environment for relief from chronic asthma, a form of therapy consisting only of ketogenic and low carbohydrate diets was tried, and the results are recorded in this communication.

MATERIAL AND METHOD

The material for this study is based on observations of fifteen children afflicted with chronic asthma (twelve sensitive and three nonsensitive to protein), ranging

* Submitted for publication, Jan. 6, 1930.

* From the Children's Asthma Clinic, Mount Sinai Hospital, Department of Pediatrics, Dr. Béla Schick, Director, and from the Department of Dietetics, Adeline Wood, supervising dietitian.

1. Peshkin, M. M.: Asthma in Children: IX. The Rôle of Environment in the Treatment of a Selected Group of Cases; a Plea for a "Home" as a Restorative Measure, Am. J. Dis. Child. **39**:774 (April) 1930.

in age from 3 to 15 years. The average age for the onset of asthma was 3.73 years, and the average age of the patients when first seen was 6.5 years. The average duration of asthma prior to treatment with the ketogenic diet was approximately five years.

Eleven of the fifteen children commenced the special dietary regimen in the winter, a season during which the symptoms of asthma are generally aggravated. The remaining four children began it in the spring of the year. The patients were under observation for periods ranging from five to ten months.

Six of the fifteen children gave a history of having, or of having had, eczema. Another four had recurrent urticaria, and one had intestinal allergy.

METHOD

The procedure employed in this investigation was as follows: The age, the weight and the total and sitting heights of each child were determined. It was found that the estimation of the food requirement in any given case was more easily and quickly determined from a formula used in the Pirquet[2] or "Nem" system of feeding than with any other method.

Every effort was made to include in the diet the amounts of calcium, phosphorus,[3] iron and vitamins necessary for growth and development. In the diets with a ketogenic-antiketogenic ratio of 3:1 in which only 15 or 20 Gm. of carbohydrates was allowed, some difficulty was encountered. At least one-half glass of milk and one-half orange were included in each diet. Milk, cheese and vegetables were given for their high calcium content. Plenty of vegetables were allowed. Calcium in the form of calcium lactate or vitamins in the form of cod liver oil were not added. No drugs were permitted. Changes in environment were not recommended, for obvious reasons. A history of intolerance or the exhibition of positive skin reactions to various food substances prompted the exclusion of these foods from the diets of the children not only for some time prior to the institution of the special dietary treatment but also throughout the period of ketogenic diet. The ketogenic diet should not be confused with the elimination diets of Rowe[4] and Dale and Thornberg[5] which have for their

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2. Pirquet, Clemens: An Outline of the Pirquet System of Nutrition, Philadelphia, W. B. Saunders Company, 1922. The Pirquet system of feeding has for its unit the "nem," which is equivalent to 1 cc. of human or cow's milk. One ounce of milk (20 calories) is equivalent to 30 nems. One nem is therefore the equivalent of two thirds of a calorie. The food requirement in the diet is determined by multiplying the square of the sitting height (in centimeters) by the desired number of decinems. Thus, a diet of 3.5 decinems (0.35 nems) for a child whose sitting height is 70 cm. is calculated as follows: $70 \times 70 = 4{,}900$ nems; $4{,}900 \times 0.35 = 1{,}715$ nems. The corresponding number of calories is $1{,}715 \times \frac{2}{3} = 1{,}143$. A maintenance diet for children is calculated at 4.5 decinems and a basal requirement diet at 3 decinems. Some children, because of overactivity, require diets of higher caloric value (from 5 to 6 decinems).

3. Sherman, H. C.: Chemistry of Food and Nutrition, New York, The Macmillan Company, 1928. The average growing child requires approximately 1 Gm. of calcium and 1.4 Gm. of phosphorus in the daily diet.

4. Rowe, A. H.: Food Allergy, Its Manifestations, Diagnosis and Treatment, J. A. M. A. **91**:1623 (Nov. 24) 1928.

5. Dale, J., and Thornberg, H. D.: Diets for the Identification of Food Allergies, J. A. M. A. **93**:505 (Aug. 17) 1929.

purpose the identification of food allergies in a patient refractory to the skin tests along with a history negative for food intolerance.

Detailed instructions were given to the mother by the dietitian concerning the preparation of the diet menus, i. e., the size of the portions, the weights and volume of food, substitution formulas, etc. The diets were made as appetizing as possible.

From several days to one week prior to the institution of the dietary treatment, an account of the quantity and kind of food eaten daily by the child was recorded in detail. From this record were calculated the carbohydrate, protein and fat values in grams, the total caloric value and the ketogenic-antiketogenic ratio.[6] These results are set forth with other details in table 1.

$$\frac{\text{Fatty acids}}{\text{Dextrose}} = \frac{\text{Ketogenic}}{\text{Antiketogenic}} = \frac{0.44\ P + 0.9\ F}{C + 0.58\ P + 0.1\ F}$$

TABLE 1.—*Estimated Daily Food Intake by Children with Chronic Asthma Prior to the Institution of Treatment with the Ketogenic Diet*

Patient	Age, Year	Weight, Kg.	Total Height, Cm.	Sitting Height, Cm.	Decinems*	Carbohydrate, Gm.	Protein, Gm.	Fat, Gm.	Total Calories	Ketogenic-Antiketogenic Ratio*
1	10	25.9	132.5	71	3.6	120	45	60	1,200	1:2
2	10	31.3	136.0	71	4.2	167	47	63	1,423	1:2.5
3	15½	42.7	147.5	79	4.2	196	60	80	1,740	1:2.5
4	15½	41.3	102.5	87	3.0	160	45	70	1,450	1:2
5	3½	17.7	101.0	58	6.0	180	40	50	1,330	1:3
6	5	20.4	115.0	61	6.0	165	55	65	1,465	1:2.5
7	13	50.9	155.0	82	3.2	135	50	80	1,460	1:2
8	14¾	48.2	157.5	81	3.6	175	45	75	1,555	1:2.5
9	4¾	16.3	102.5	57.5	3.7	92	20	41	817	1:2.5
10	10	21.3	127.5	70	5.0	175	40	90	1,670	1:2
11	8½	28.8	125.0	70.5	4.0	135	40	70	1,330	1:2
12	8½	24.0	127.5	71	5.0	150	60	90	1,650	1:2
13	4	17.7	100.0	59	6.0	150	40	70	1,390	1:2
14	6	21.8	120.0	64	3.2	85	29	46	870	1:2
15	2⅔	14.5	92.5	54	5.7	100	44	50	1,107	1:2

* Figures are approximate. For the determination of decinem, see footnote 2, and for the diet ratio see footnote 6.

From table 1 it may be seen that nine children were living on diets the daily rations of which were below the maintenance requirement (4.5 decinems). Seven of the children in this series were found to be underweight. It is of interest, however, to note that all of these children were taking a diet relatively high in carbohydrate. Nine children were on a diet with an approximate ketogenic-antiketogenic ratio of 1:2, five were on diets with a ratio of 1:2.5 and one was on a diet with a ratio of 1:3.

Routine Employed in the Treatment with the Ketogenic Diet.—With the sitting height of the child determined, a diet of 3.5 decinems was computed and converted into calories. The child was placed on this calculated diet with a ketogenic-antiketogenic ratio of 1:1.5 for two days. At the end of this time, the ratio was changed to 1:1. In another two days, the caloric intake was increased to 4 decinems, and the diet ratio to 1.5:1. Several days later, the child was placed on a maintenance diet (4.5 decinems) with a ratio of 2:1. Again in a few days, the ratio was increased to 2.5:1 and finally to the maxi-

6. Woodyatt has proposed a formula based on the equimolecular weights of dextrose and fatty acids.

mum of 3:1, while the caloric intake was kept at the maintenance level. Ten per cent protein was allowed.

The diets of all the children were maintained for periods ranging from four to ten months. One child was placed on a diet of 5 decinems with a ratio of 2:1, and at the end of the second week the ratio was reduced to 1:1, which was maintained throughout the dietetic experiment (five months). This was done in order that we might observe the effect on the asthma of a diet relatively low in carbohydrate in the absence of ketosis. In this instance, the ratio of the original home diet was 1:2. In three cases, diets of the maximum caloric value were given from the start for the purpose of determining whether or not the initial diets of low caloric value were essential in obtaining satisfactory results.

EFFECTS OF THE DIETS ON ASTHMA

Table 2 is a summary of the results of treatment of fifteen children with the ketogenic and low carbohydrate diet, with other essential data.

Prior to the institution of this special dietary regimen these children (table 2) were under observation and treatment for varying periods as follows: two children for five years, two for four years, six for from one to three years, and five for less than one year.

Table 2 shows that slight improvement from asthma occurred in nine children at the end of the first week under the special dietary regimen. At the end of the second week of treatment, ten children showed moderate improvement and three marked improvement or relief from asthma. At the end of the third week, fourteen children, or 93 per cent of the series, manifested moderate to marked improvement or relief from asthma.[7]

The subsequent month to month progress of each child under the dietary regimen is readily obtained from table 2. Of the two children observed for ten months, one showed moderate to marked improvement and the other only slight improvement. The latter child was the only one (no. 4) of the series who failed to show a favorable response during the first month of treatment. Three children were observed for nine months; one of these children showed continued marked to moderate improvement, while the other two had an aggravation of the asthma in the fifth and the eighth months, respectively. Of the two children observed for eight months, one continued to show moderate improvment, and the other manifested a return of symptoms ("slipping") in the fourth month. The three children observed for seven months continued to show marked improvement or relief from asthma. Of the five children under treatment for periods ranging from four to six months, three showed evidences of "slipping" in the third, fourth and fifth months,

7. In a series of unpublished observations, marked improvement from asthma was elicited at the end of the first week in cases in which diets with ratios of 1:1, 2:1 and 3:1 were given at intervals of two days, respectively. The sudden shift from a home diet to one with a ratio of 3:1 is also under investigation.

TABLE 2.—*Results of the Treatment with the Ketogenic and Low Carbohydrate Diet in Fifteen Children with Chronic Asthma of the Refractory Type*

Patient	Age,* Year	Age First Seen, Year	Age of Onset of Asthma, Year	Duration of Asthma, Year	Results of Treatment **													Weight, Kg.	
					First Month				Subsequent Months									At Onset of Diet Treatment	At End of Diet Treatment
					1 w†	2 w	3 w	4 w	2	3	4	5	6	7	8	9	10		
1	10	9	1	9	+	++	+++	+++	+++	++	++	+	+	+	+	0		25.9	27.7
2	10	9½	9	1	+	+++	+++	+++	+++	++	++	+++	+++	+++	+++	++	++	31.3	36.3
3	15½	11	7	8½	0	++	+++	+++	+++	+++	+++	++	++	++	+§	0		42.7	45.4
4¶	15½	12	7	8½	0	+	0	0	+	++	++	+	+	+	++	++	+	41.3	44.9
5	3½	1	½	3	+	++	+++	+++	+++	+++	+++	+++	+++	+++	++	++		17.7	20.4
6	5	4	3	2	+	+++	+++	+++	+++	0	0	+	#					20.4	20.0
7	13	8	4	9	+	++	+++	++	+++	+++	++	+	++	+	0			59.9	55.0
8	14¾	13	6	8¾	0	++	++	++	+++	+++	+++	++	++	++§	++			48.2	51.4
9¶	4¾	4	3	1¾	+	++	+++	+++	+++	+++	+++	+++	+++	++				16.3	17.7
10	10	4½	4	6	0	++	+++	+++	+++	+++	+++	+++	+++	+++				21.3	32.2
11¶	8½	7¾	4	4½	+	+++	+++	+++	+++	+++	+++	+++	+++	+++				28.8	30.9
12	8½	8	2½	6	+	++	+++	+++	+++	++	+++	+						24.0	26.4
13‡	4	1	½	3½	0	+	++	+++	+++	+++	+++	+++						17.7	19.0
14	6	4	3½	2½	+	++	+++	++	++	++	+							21.8	22.7
15	2⅔	2	⅔	2	0	+++	+++	+++	+++	+++	+++							14.5	15.9

* Age when dietary regimen was begun.

** Slight improvement = +; moderate improvement = ++; marked improvement or relief from asthma = +++, and no improvement = 0.

† w = week.

‡ For the first two weeks the diet ratio was 2:1; thereafter, the ratio was reduced and maintained at 1:1.

§ Taking home diet.

¶ Protein nonsensitive.

#Sent to "convalescent home" for four months, where he was free from asthma and gained 1.8 Kg.

respectively; and the remaining two continued to manifest marked improvement or relief from asthma.[8]

It is thus apparent that the marked control of the asthmatic condition noted at the end of the third and fourth weeks in the fourteen cases was not permanent. After this period, six patients maintained their improved condition for periods varying from two to seven months before relapses ensued. The asthma in the latter cases, as a rule, was not so severe and prolonged as in the period prior to the special dietary treatment. The cause and prevention of a relapse to the asthmatic state warrant further investigation. The remaining eight patients, or 53 per cent of the series, continued to maintain moderate to marked improvement or relief from asthma for periods varying from four to ten months.

The first signs of improvement noted were the diminution or disappearance of dyspnea and heaviness in the chest. Wheezing was soon less noticeable, and the attacks of asthma were milder and less frequent. The cough was less troublesome or gone. The child looked better, and the pinched appearance was replaced by a pleasant facial expression. The nocturnal wheeze was slightly present, if at all, and sleep was undisturbed. Later the cheeks became noticeably pink, and the posture was improved. The child became more alert and active and could run up and down the stairs without inducing a wheeze or dyspnea. Such striking improvement from severe asthma of the refractory type was observed with no other treatment, except hospitalization or change of environment.[1]

The case to be reported is of special interest because of the marked gain in weight and because of the intensity and long duration of the asthma, which was finally controlled with the ketogenic dietary regimen.

REPORT OF CASE

M. W. (patient 10, table 2), a girl, was first seen on May 15, 1923, when 4½ years of age, with a history of asthma the onset of which occurred eight months previously. There was no personal history of eczema, urticaria or angioneurotic edema. The antecedent family history was positive for allergy, the paternal grandfather having had asthma. When first seen, the patient appeared malnourished and weighed 31½ pounds (14.3 Kg.). The results of physical examination were otherwise negative except for the usual signs of asthma in the chest. Roentgenoscopy of the chest showed no definite abnormality in the lungs. A complete series of protein skin tests (scratch and intradermal technics) showed positive reactions to barley, radish, mustard and house dust. The Pirquet test was negative. The intradermal test was negative up to a concentration of 1 mg. of tuberculin. The blood count was normal. The patient was given appropriate dietetic and environmental treatment. Tonsillectomy and

8. The ketogenic diet treatment was administered to two adults with severe chronic asthma, of the type nonsensitive to protein, with no improvement. Acetonuria, however, resulted.

adenoidectomy were performed during the first year of observation, with no apparent benefit. Later, attacks of asthma became progressively more frequent, prolonged and intense. A series of nonspecific injections of sterile skimmed milk was administered, with little or no improvement. Ten months after the patient's admission to the clinic, she contracted acute lobar pneumonia with involvement of both lower lobes. During this illness of three weeks and for a subsequent month, she remained free from asthma. Then attacks recurred at intervals of from two to three weeks with spells of wheezing intervening. Another course of nonspecific injections (milk) was given. Later, a stock house dust was employed, as well as the extract made from the dust collected in the patient's home. General irradiations of the body by ultraviolet ray were also employed. Finally, injections of *Crotalus atrox* (nonspecific therapy) up to a concentration of 1.5 mg. were administered. In spite of all of these various forms of therapy, the patient continued to have severe asthma.

This condition existed for six years. The child was unable to attend school. On Feb. 14, 1929, she reported with a history of having had continual asthma for the three previous months.

On March 9, treatment with the ketogenic dietary regimen was commenced. The child was 10 years of age, the total height 127.5 cm. (51 in.) and the sitting height 70 cm. She was emaciated, weighing 47 pounds (21.3 Kg.), being 15 pounds (6.8 Kg.) underweight. Her posture was poor, and she appeared chronically ill. The anteroposterior measurement of the chest was increased above the normal.

The "home" diet that she had been taking was estimated to consist of 175 Gm. of carbohydrate, 40 Gm. of protein and 90 Gm. of fat, or 1,670 calories (5 decinems) with a ketogenic-antiketogenic ratio of 1:2. She commenced the dietary regimen with a diet of 1,275 calories (3.5 decinems) with a ratio of 1:1. Within a week, the diet was increased to 1,310 calories (4 decinems) with ratios of 1.5:1 and 2:1, respectively. At the end of two and one-half weeks, the patient was on a daily ration of 1,480 calories (4.5 decinems) with a ratio of 3:1.

At the end of the third week of dietary treatment, the child showed remarkable improvement. She was free from attacks of asthma and was able to get about with ease. At the end of the first month, she had no wheeze and had gained 2 pounds (0.9 Kg.). It may be mentioned here that for the entire year prior to this treatment, she showed a gain of only 1 pound (0.5 Kg.). The urine showed a moderate reaction to acetone with the diet ratio of 2:1 and a marked reaction with ratios of 2.5:1 and 3:1. Improvement continued during the second month; at this time, the patient was put on a diet of 1,660 calories (5 decinems) with a ratio of 3:1, with a resultant gain in weight of 7½ pounds (3.4 Kg.). Acetonuria persisted. It is of interest to state that this child previous to the dietary regimen was subject to frequent spells of "acidosis" with and without attacks of asthma. Now, with a ketosis induced by the ketogenic diet, she remained free from symptoms of "acidosis" and asthma.

The total period of observation of this patient under the treatment with the ketogenic diet was seven months. She had no attacks of asthma during this time, but had an occasional spell of wheezing at night. On October 8, she weighed 71 pounds (32.2 Kg.), showing a gain of 24 pounds (10.9 Kg.). Beginning with the seventh month, the diet ratio was reduced to 2:1, after which no acetone in the urine could be demonstrated. She was still on this diet at the time of writing, felt well and was attending public school for the first time in her life.

Table 3 shows, with other essential data, three of the menus with different ketogenic-antiketogenic ratios given to the patient in the case reported.

EFFECT OF THE DIET ON ACETONE IN THE URINE

The time of appearance of acetone in the urine (qualitative estimation) varies with the child. At some time during the first month of

TABLE 3.—*Three of the Menus Given to Patient M. W. (10, Table 2) * During Treatment with the Ketogenic Diet*

1:1 Ratio		2:1 Ratio		3:1 Ratio	
Grams	Food	Grams	Food	Grams	Food
	Breakfast		**Breakfast**		**Breakfast**
50	½ orange	50	½ orange		1 egg
	1 Uneeda cracker	100	½ glass milk	50	¼ glass milk
200	1 glass milk	50	¼ glass cream 40%	100	½ glass cream 40%
				12	1 square butter
	Dinner		**Dinner**		**Dinner**
	1 cup broth		1 cup broth		1 cup broth
		70	⅓ cup meat, fish 70 or chicken	70	⅓ cup meat, fish 70 or chicken
100	½ cup vegetables 3-5%	75	⅓ cup vegetables 3-5%	75	⅓ cup vegetables 3-5%
12	1 square butter	12	1 square butter	18	1½ squares butter
200	1 glass milk	50	¼ glass cream 40%	50	¼ glass cream 40%
	3 P.M.		**3 P.M.**		**3 P.M.**
200	1 glass milk	100	½ glass milk		
		50	¼ glass cream 40%		
	Supper		**Supper**		**Supper**
	1 cup broth		1 cup broth		1 cup broth
20	¼ pkg. cream cheese	30	⅓ pkg. cream cheese	30	⅓ pkg. cream cheese
100	½ cup vegetables 3-5%	75	⅓ cup vegetables 3-5%	75	⅓ cup vegetables 3-5%
18	1½ squares butter	12	1 square butter	18	1½ squares butter
200	1 glass milk	50	¼ glass cream 40%	50	¼ glass milk
50	¼ glass cream 40%			50	¼ glass cream 40%
	1 Uneeda cracker				

Summary		Summary		Summary	
Ratio	1:1	Ratio	2:1	Ratio	3:1
Carbohydrate	70	Carbohydrate	30	Carbohydrate	15
Protein	35	Protein	35	Protein	35
Fat	86	Fat	125	Fat	145
Calories	1,194	Calories	1,385	Calories	1,505
Decinems	3.5	Decinems	4	Decinems	4.5
Calcium	1.319	Calcium	0.795	Calcium	0.689
Phosphorus	1.046	Phosphorus	0.766	Phosphorus	0.753
Iron	0.00627	Iron	0.00550	Iron	0.00609
Vitamin A	+++	Vitamin A	+++	Vitamin A	+++
B	++	B	++	B	++
C	+	C	+	C	+

* Sitting height 70 cm.

treatment, eleven children showed the presence of acetone. Of these children, six gave slightly positive reactions on a diet with a ketogenic-antiketogenic ratio of 1.5:1, three on a diet with a ratio of 2:1 and the remaining two on a diet with a ratio of 2.5:1. Only five (1, 2, 10, 12 and 14, table 2) of these eleven children showed moderate to marked reactions to acetone during the first month with the maximum diet ratio of 3:1. These five children and one other (7, table 2) ate only the foods permitted on the diet menus. The other children adhered less rigidly

to the prescribed diets, taking an extra Uneeda cracker or a slice of toast and at times additional fruit.

During the subsequent months, six children (1, 2, 5, 10, 12 and 14, table 2) showed repeatedly moderate to marked traces of acetone in the urine, while four children (6, 11, 13 and 15) showed none. In the latter cases, no attempt was made to induce acetonuria with higher diet ratios (3.5 : 1 and 4 : 1).

It was observed that when the children with acetonuria began to have a return or an aggravation of the symptoms of asthma, a diminution or disappearance of the acetone took place. When a child recovered from a spell of wheezing or a mild attack of asthma, the return of acetone in the urine was delayed. One child (no. 1), with a persistent acetonuria, failed to show acetone when severe asthma returned early in the ragweed pollen season, in spite of the fact that a diet with a ratio of 3 : 1 was continued for another month.

The experiment of reducing the diet ratio from 3 : 1 to 2 : 1 was tried on three children who were markedly improved or relieved from asthma and in whom marked acetonuria had existed for several months. The marked improvement or relief from asthma continued in all three patients in spite of the elimination of ketosis. This observation seems to be of clinical importance, for if satisfactory results can be maintained with reduced ratios (2 : 1 or even 1 : 1), the difficulty of getting children to continue these diets over extended periods of time will be largely overcome. A diet relatively low in carbohydrate (50 Gm.) is more readily taken than a ketogenic diet (15 Gm. of carbohydrate) with a ratio of 3 : 1.

It seems evident from the urinary observations that acetone, per se, does not wholly account for the marked relief from asthma, experienced by the majority of the patients in this series. It is evident, also, that some of the children who were supposed to be on a diet ratio of 3 : 1 were taking not more than a ratio of 2 : 1. In other words, they were actually on a diet relatively low in carbohydrate and high in fat.

EFFECT OF THE DIET ON WEIGHT

At the end of the first month of the dietary regimen, six children showed unchanged weights. Three children had gained approximately 2 pounds (0.9 Kg.) each and two had lost weight. Four children showed a loss of from 1 (0.4 Kg.) to 2 pounds (0.9 Kg.) during the first two weeks, but regained the loss by the end of the first month. During the subsequent months, thirteen of the children showed substantial increases in weight, the average increase being 6.6 pounds (3 Kg.). One girl, 13 years of age, who was 23 pounds (10.4 Kg.) overweight, showed a loss of 9 pounds (4.1 Kg.) in eight months on

a diet above maintenance level (5.5 decinems) with a ratio of 3:1 and improvement from asthma. However, gain in weight, as a rule, accompanied clinical improvement. When a child began to "slip" and the symptoms of asthma returned or became aggravated, loss of weight and appetite followed. Subsequent experience justifies the statement that the use of maintenance diets or diets of higher caloric value with a ketogenic ratio in the treatment of a child with chronic asthma who is underweight, usually results in an appreciable gain of weight by the child after a period of four months, while in the case of a child who is obese, the use of such diets usually leads to a loss of weight in spite of the fact that both types of children have improved or have been relieved from asthma. Further investigations are being carried out for the purpose of ascertaining, if possible, an explanation for this interesting seeming paradox.

EFFECT OF THE DIET ON POLLEN SENSITIVENESS

Four of the children of this series were sensitive to ragweed pollen, in addition to being sensitive to food and other inhalant substances; two of these children were also sensitive to timothy. A ketogenic diet with a ratio of 3:1 was maintained before and during the pollen seasons and in each instance asthma returned or became aggravated and were accompanied by symptoms of hay-fever during the season. None of these children received pollen treatment during 1929.

One child, not included in this series, was sensitive to many substances besides ragweed pollen. Preseasonal treatment against ragweed pollen was commenced in April, 1929. In May, the patient developed a troublesome cough with nocturnal wheezing which could not be accounted for. These symptoms became progressively worse, and in July the ketogenic diet was commenced and continued with pollen therapy to the end of September. The patient was relieved from all symptoms and continued to remain so after the first week of the dietary regimen.

Three children, with only hay-fever of the ragweed type, not included in this series, were also studied. One boy of 12 years was previously treated for three years with preseasonal injections of pollen extract, with satisfactory results. On Aug. 6, 1929, the child was placed exclusively on the dietary regimen, receiving at intervals of two days, ratios of 1:1, 2:1 and 3:1, respectively. The latter ratio was continued through August and part of September. There was moderate to marked acetonuria. However, severe hay-fever ensued, and pollen treatment was instituted to control the symptoms. Another child, a younger brother, was given the ketogenic diet at the same time and also did poorly during the pollen season. A third child, a boy of 9 years, commenced on the dietary regimen during the height of the hay-fever season

(August 29). He was taking a diet above the maintenance level (5 decinems) with a ratio of 3:1, which was maintained for one month. The urine showed marked traces of acetone. The mother said that the boy showed some improvement over the previous year, when no treatment of any kind was given.

From these results it appears that the ketogenic diet alone does not offer much promise of relief in hay-fever with or without asthma, but no final statement can be made until a larger number of cases is studied. However, the suggestion of administering specific pollen treatment in conjunction with the ketogenic diet in certain cases of asthma, may be borne in mind.

EFFECT OF THE DIET ON THE DERMATOSES

Six children in this series gave a history of eczema occurring during infancy. In three, the eczema had cleared several years before the dietary treatment was started, and in the other three, the eczema was recurrent in type. In two of the latter, the eczema became definitely aggravated on the diet high in fat. These two children demonstrated sensitivity to many substances, particularly to foods. The eczematous condition was treated with the usual ointments, with good results in spite of the existing ketosis.

Four of the children had recurrent urticaria. With the clearing up of the asthma, the itch and rash in two became aggravated. Later, an impetigenous eruption developed in one of these children.

Observations were made on three children with reference to the effect of ketosis on the protein skin reactions. No change in the skin reactions to food, inhalant substances and pollen in any of these children was observed even though they were markedly improved or relieved from asthma.

EFFECT OF THE DIET ON ASTHMA DURING INTERCURRENT INFECTIONS AND IN OTHER CONDITIONS

Intercurrent infections, such as grip and other respiratory infections, in some cases precipitated symptoms of asthma, milder, however, than those occurring in the prediet period.

Two children indulged in food to which they were specifically sensitive, and an attack of asthma resulted in each instance in spite of the ketogenic diet.

Two other children after having shown moderate to marked improvement from asthma for six and seven months, respectively, were at the end of these periods placed back on their original home diets. In one, symptoms of asthma became definitely aggravated, while in the other there was no change.

MISCELLANEOUS OBSERVATIONS

No untoward effects were observed in the children of this and subsequent series while under the ketogenic dietary regimen. Several children complained of hunger, which was readily relieved with an increase in the caloric value of the diet. Nausea and vomiting did not occur. Four children became constipated. Several others complained when the high fat diet was continued over a period of months, in spite of the fact that menus were changed and foods made more palatable. This diet is rather costly for this class of patients because of the daily requirement of large quantities of sweet cream and butter.

COMMENT

The reason for the beneficial effect resulting from the ketogenic diet in the treatment of certain conditions is not known. Several theories have been advanced making different mechanisms responsible for the favorable results obtained, but none of these theories has been generally accepted. In recent years, the ketogenic diet has been largely employed in the treatment for epilepsy in childhood. The literature is replete with comprehensive communications on this special dietary treatment of epilepsy; it includes reports by Wilder,[9] Peterman,[10] Talbot and his associates,[11] Lennox and Cobb [12] and Helmholz.[13]

In certain cases, idiopathic epilepsy is regarded by some workers as an allergic phenomenon and is referred to by Schick [14] as an "asthma of the brain." The application of the ketogenic diet in the treatment for asthma in childhood in certain cases appears therefore not to be without foundation.

All of the children in this series, prior to the dietary treatment, were living on diets with ketogenic-antiketogenic ratios ranging from 1:2 to 1:3 (high in carbohydrate, low in fat). The change to a diet ratio of 3:1 (low in carbohydrate, high in fat) shifted the balance in the opposite direction. The rapid improvement or relief from asthma observed following treatment with the ketogenic diet exclusively in

9. Wilder, R. M.: The Effects of Ketonuria on the Course of Epilepsy, Mayo Clin. Bull. **2**:307, 1921.

10. Peterman, M. G.: The Ketogenic Diet in the Treatment of Epilepsy, Am. J. Dis. Child. **28**:28 (July) 1924.

11. Talbot, F. B.; Metcalf, K. M., and Moriarty, M. E.: A Clinical Study of Epileptic Children Treated by Ketogenic Diet, Boston M. & S. J. **196**:89 (Jan. 20) 1927.

12. Lennox, W. G., and Cobb, S.: Epilepsy from the Standpoint of Etiology and Treatment, Medicine **7**:105 (May) 1928.

13. Helmholtz, H. F.: The Treatment of Epilepsy in Childhood; Five Years' Experience with the Ketogenic Diet, J. A. M. A. **88**:2028 (June 25) 1927.

14. Schick, Bela: Personal communication to the authors.

children with chronic asthma of the refractory type is possibly brought about by some mechanism which involves a physicochemical change in the cells and blood of the patient thereby inducing a partial or completely restored "physicochemical" [15] or "allergic balance." [16] This physicochemical balance may be associated with changes in the surface tension of various colloids, hydrogen-ion concentration, calcium, phosphorus, cholesterol, sodium chloride and other chemical elements. McQuarrie and Keith [17] found that in children under treatment with the ketogenic diet, attacks of epilepsy diminished or disappeared when the p_H of the blood was between 7.33 and 7.41 or lower. The attacks, however, returned with the administration of alkalis or after the withdrawal of the diet or when p_H was above 7.41 (on the alkaline side). In a recent communication, McQuarrie [18] emphasized the importance of the water balance and favored a diminution of the water intake in the treatment for this condition. These chemical changes may be nothing more than secondary observations incident to the disease and may be expressions of a physicochemical change.

Patients with certain diseases have been successfully immunized with specific vaccines via the alimentary tract. Early immunization of infants against tuberculous infection by the ingestion of the Calmette preparation (B.C.G.) has been carried out with apparent success. Peptone, ingested by patients with food allergy for purposes of nonspecific desensitization, is not without value. The ketogenic diet, on account of its extreme formula, is a dietary "stranger" to the allergic person; and, in our opinion, this diet can be considered, for children, at least, as a form of nonspecific therapy capable of inducing physicochemical change via the alimentary tract.

CONCLUSIONS

1. In a series of fifteen children (twelve sensitive and three nonsensitive to protein) ranging in age from 3 to 15 years, the asthma remained severe, persistent and of long duration in spite of treatment according to accepted standards of modern investigation and management. These children had been under observation for an average of two and one-fifth years when selected for treatment with the ketogenic

15. Peshkin, M. M.: Asthma in Children: III. The Incidence and Significance of Various Diseases and Infections, and of Tonsillectomy and Adenoidectomy, Am. J. Dis. Child. **33**:880 (June) 1927.

16. Vaughan, W. T.: Interaction of Specific and Nonspecific Factors in Allergic Disease, Virginia M. Monthly **51**:472 (Nov.) 1924.

17. McQuarrie, I., and Keith, H. M.: Experimental Study of the Acid-Base Equilibrium in Children with Idiopathic Epilepsy, Am. J. Dis. Child. **37**:267 (Feb.) 1929.

18. McQuarrie, I.: Epilepsy in Children; the Relationship of Water Balance to the Occurrence of Seizures, Am. J. Dis. Child. **38**:451 (Sept.) 1929.

(and low carbohydrate) diets. No drugs, injections or other therapeutic measures were employed. However, the various foods known to cause symptoms of allergy in these patients were eliminated not only from their former diets, but also from the ketogenic diets.

2. The estimated daily amount of food consumed by these children prior to the institution of the ketogenic diet regimen showed that they were all living on diets relatively high in carbohydrate. The approximate ketogenic-antiketogenic ratios of the home diets ranged from 1 : 2 to 1 : 3.

A maintenance diet or one of higher caloric value with a maximum ketogenic ratio of 3 : 1 was reached in all the cases (except one) within three weeks, and thereafter this level was maintained for periods ranging from four to ten months. Ten per cent protein was allowed.

3. At the end of the third week of treatment with the dietary regimen, fourteen children, or 93 per cent of the series, manifested moderate to marked improvement or relief from asthma. These improved states were maintained for another two months. Thereafter, and up to the tenth month, 53 per cent of the patients were considered moderately to markedly improved or relieved from asthma.

4. The ketogenic and low carbohydrate diets alone do not appear to offer much promise of relief from pollen asthma (four cases in this series) or hay-fever (three cases not included in this series). However, in pollen asthma, the administration of pollen treatment in conjunction with the ketogenic diet may prove of value.

5. Ketosis, per se, apparently does not account for the results obtained, since definite improvement or relief from asthma also occurred in some children in whom acetone in the urine could not be demonstrated.

Some of the children who were doing well on a ketogenic ratio of 3 : 1 were later actually taking ratios as low as 1.5 : 1 with continued benefit. In other words, they were finally on a relatively low carbohydrate-high fat diet, below the threshold of ketosis.

6. The use of a maintenance diet or one of higher caloric value with a ketogenic ratio of 3 : 1 in the treatment of a child with chronic asthma who is underweight usually results in an appreciable gain in weight by the child after a period of four months, while in the case of a child who is obese, the use of such a diet usually results in a loss of weight, in spite of the fact that both types of children have been improved or relieved from asthma. This is an interesting seeming paradox.

7. Children with asthma and recurrent eczema on a ketogenic diet showed definite improvement from asthma but aggravation of the eczema. However, the children who have been free from eczema for

several years prior to the institution of the low carbohydrate-high fat diet do not have a recurrence of the rash in spite of prolonged ketosis.

Two of the four children with recurrent urticaria had an aggravation of the rash as a result of the dietary regimen.

8. The estimation of the food requirement in any given case was more easily and quickly determined from a formula used in the Pirquet [2] system of feeding than with any other method.

9. The rapid control of asthma or relief from it observed following treatment with the ketogenic diet exclusively is possibly brought about by some mechanism which involves a physicochemical change in the cells and blood of the patient thereby inducing a partially or completely restored "physicochemical" [15] or "allergic balance." [16] Recent experimental evidence lends support to this conception.

The ketogenic diet, on account of its extreme formula, is a dietary "stranger" to the allergic person and, in our opinion, may be considered, for children, as a form of nonspecific treatment capable of inducing physicochemical change via the alimentary tract.

10. In this series of selected children with chronic asthma refractory to various forms of modern treatment, the ketogenic and relatively low carbohydrate-high fat diets alone have proved efficacious to the extent that the chronic asthmatic state in the majority of instances was controlled or entirely cleared up, at least for a sufficient period of time to permit such a child to get its bearings.

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Case Reports

IDIOPATHIC CARDIAC ENLARGEMENT ASSOCIATED WITH STATUS THYMICOLYMPHATICUS *

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Enlargement of the heart in infancy and in childhood, without any anatomic basis, has been described under the terms of idiopathic cardiac hypertrophy, dilatation or enlargement. A close review of some of the cases reported under these various headings reveals the fact that not all of the cases can be called idiopathic, because of the presence of renal lesions in some and of coarctation of the aorta in others. More careful microscopic examination of the heart also revealed the presence of lymphocytic infiltrations in the myocardium itself. Cases have also been reported with myocardial round cell infiltration in association with status thymicolymphaticus (Ceelen,[1] Blühdorn [2]), while other cases have been reported in which status thymicolymphaticus or thymic enlargement was present in addition to the cardiac enlargement without myocardial round cell infiltration (Oberndorffer,[3] Howland [4]). There remains, however, a group of cases in which the only pathologic change is the enlargement of the heart. Thus, on the basis of the cases reported in the literature, one can classify idiopathic enlargement of the heart in infancy and in childhood as follows:

1. Idiopathic enlargement with status thymicolymphaticus and with round cell infiltration in the myocardium.
2. Idiopathic enlargement with status thymicolymphaticus without round cell infiltration in the myocardium.
3. Idiopathic enlargement with round cell infiltration in the myocardium only.
4. Idiopathic enlargement without any other anatomic change, either grossly or microscopically.

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1. Ceelen: Klin. Wchnschr. **22**:27, 1916.
2. Blühdorn, K.: Monatschr. f. Kinderh. **29**:193 (Dec.) 1924.
3. Oberndorffer: Verhandl. d. Gesellsch. f. Kinderh. **23**:180, 1906.
4. Howland: Contributions to Medical and Biological Research, New York, Paul B. Hoeber, Inc., 1919, p. 583.

Up to 1927, Stoloff [5] collected thirty-four cases reported in the literature as idiopathic hypertrophy, enlargement or dilatation of the heart. An analysis of these cases showed that only seventeen could be considered as cases of true idiopathic enlargement of the heart. In three of the cases there was associated status thymicolymphaticus (Oberndorffer,[3] Howland [4]). Six cases reported as idiopathic hypertrophy revealed lymphocytic infiltration in cardiac muscle. Four cases were reported subsequent to the thirty-four cases already mentioned, one by Stoloff, two by Oberhammer [6] and one by Cathola;[7] the last three were cases of true idiopathic enlargement, while that first mentioned revealed lymphocytic infiltration in the cardiac muscle on microscopic examination.

The case herein reported is one of the group of myocardial enlargements associated with status thymicolymphaticus without round cell infiltration of the cardiac musculature.

REPORT OF A CASE

History.—L. U., a white boy, aged 3 months, was admitted to the pediatric service of the Jewish Hospital on April 7, 1929, because of "blueness" of two days' duration and cough of one day's duration. The family history was essentially unimportant. The child was born at full term and weighed 6 pounds (2.7 Kg.). Delivery was not instrumental. There was no cyanosis at or after birth. He took his feedings of breast milk well for the first ten days, but had to be weaned because of lack of mother's milk. He was then given a milk and water mixture, one-half ounce of orange juice and one teaspoonful of cod liver oil. Up to the present illness, the child was apparently well.

The present illness began four days before admission, when the mother noticed that the child did not take his feedings as usual. He was restless at night and perspired profusely. Two days before admission, he became "blue in the face" during a crying spell, and on the following day, cyanosis associated with difficulty in breathing was observed. It was also noticed that there was embarrassment of respiration and whistling noises in the infant's chest. On the day of admission, he developed a nonproductive cough. There was no croup or hoarseness, nor were any convulsions observed. The bowel movements were normal. There was no vomiting or any history of a foreign body having been aspirated. On admission, the temperature was 101.4 F.; the pulse rate, 90.

Physical Examination.—Physical examination revealed a fairly well nourished and well developed infant with slight loss of skin turgor. He did not appear acutely ill, and there were no signs of respiratory embarrassment. The cervical lymph nodes were slightly enlarged. The axillary nodes were markedly enlarged, especially on the right side. The inguinal and epitrochlear nodes were slightly enlarged. The anterior fontanel measured 6 cm.; craniotabes was present, and the costochondral junctions were very prominent. No abnormal signs were present in the lungs. The heart was not enlarged to percussion; the sounds were of good

5. Stoloff: So-Called Idiopathic Enlargement of Heart in Infancy and in Childhood, Am. J. Dis. Child. **36**:1204 (Dec.) 1928.

6. Oberhammer: Ztschr. f. Kreislaufforsch. **19**:441, 1927.

7. Cathola: Bull. et mém. Soc. méd. d. hôp. de Paris **50**:1795, 1927.

quality, and no murmurs were heard. The liver and the spleen were palpable about 3 cm. below the costal margins. The knee jerks were hyperactive. No Chvostek's sign was elicited.

Course.—Five hours after admission to the hospital, while receiving his food, the child became cyanotic and had difficulty in breathing. These signs, however,

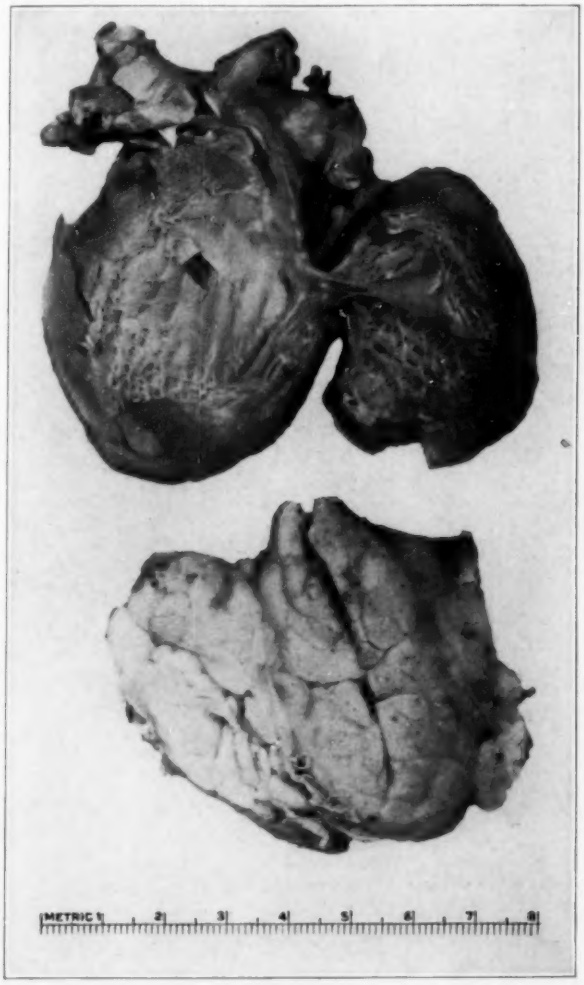

Fig. 1.—Dilatation and hypertrophy of heart; thymic enlargement.

disappeared rapidly. About one and one-half hours later, cyanosis recurred, accompanied by twitching of both arms, and in half an hour the child died.

The antemortem impression was that the child had congenital heart disease, rickets and latent tetany.

Postmortem Examination.—When the chest was opened, it was noted at once that the heart was markedly enlarged, especially to the left where it compressed the lower lobe of the left lung. It weighed 63 Gm. and was globular. The trans-

verse diameter of the heart at the base measured 6.5 cm.; the longitudinal diameter from apex to base, 6.5 cm. The right auricle appeared normal. The right ventricle was somewhat dilated but not hypertrophied. The wall was thick and measured about 5 mm. in thickness. The tricuspid valve appeared normal, its circumference measuring 5 cm. The pulmonary valves appeared normal, the circumference being 2.8 cm. The left auricle was dilated and hypertrophied. The left ventricle was very much hypertrophied and dilated; the wall was markediy

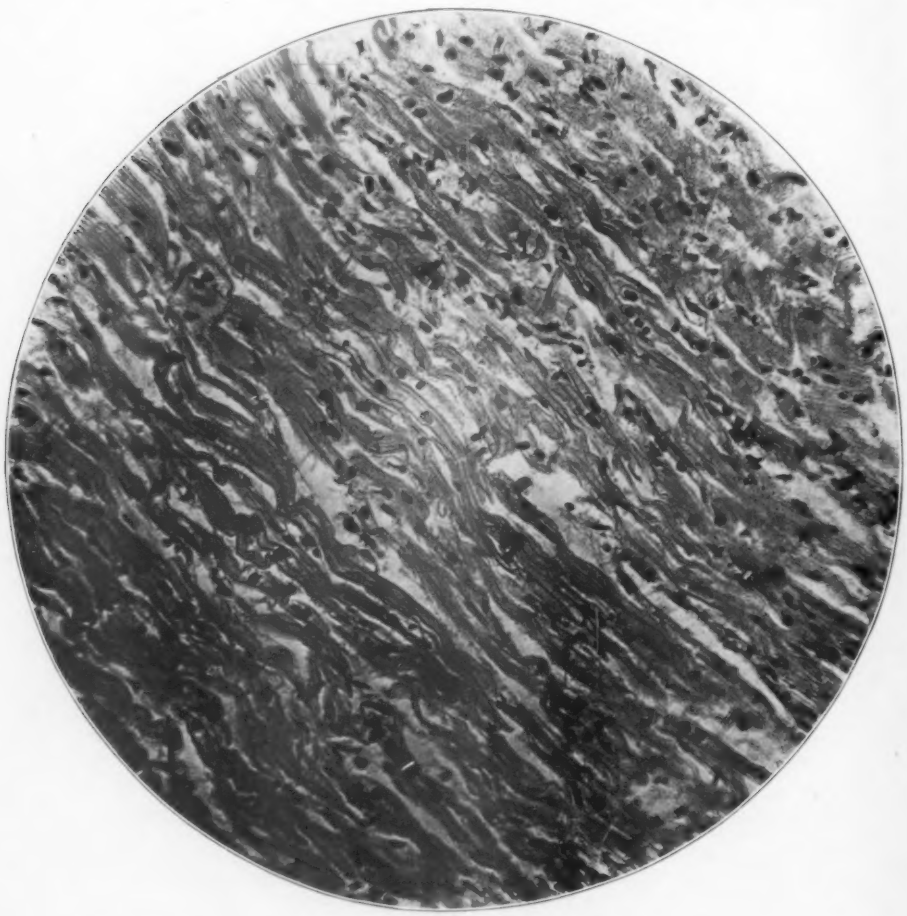

Fig. 2.—Left ventricle posterior; edema of muscle bundles; hydropic degeneration of muscle fibers and irregular distribution of fibers due to edema. Note absence of round cell infiltration and presence of short, thick fasciculi.

thickened, measuring 12 mm. in thickness. The endocardium of the left ventricle appeared grayish white and very much thickened. The aorta was normal; there was no coarctation. The coronary vessels presented no abnormalities. The ductus arteriosus and foramen ovale were closed (fig. 1).

Microscopic examination of the heart showed marked edema and moderate hypertrophy of the muscle bundles. There was some hydropic degeneration of

the muscle fibers and irregular distribution of the muscle bundles due to edema and congestion. Some of the muscle bundles were shortened and the nuclei irregularly placed. No round cell infiltration could be found in any section through the auricles, ventricles, valves and vessels (fig. 2).

There was about 300 cc. of clear, amber-colored fluid in the right pleural cavity, which on culture proved to be sterile and gave the reactions of a transudate. The lungs, liver, spleen, kidneys and brain showed passive congestion.

The thymus was large, weighing about 42 Gm., almost three times the normal weight; in addition, the mesenteric lymph nodes as well as Peyer's patches were markedly enlarged.

Signs of rickets, such as marked craniotabes, beading of the costochondral junctions and changes in the long bones were also present.

On microscopic examination, the pulmonary alveoli were filled with desquamated epithelial cells and large numbers of so-called heart failure cells. There was no pneumonia.

COMMENT

Idiopathic cardiac enlargement is found in infants from about 3 to 14 months of age. It is a rare condition, only about twenty cases having been reported in the literature up to the present time. In three of these cases, the anatomic signs of status lymphaticus were reported. The case reported here is interesting in that it showed the signs of status lymphaticus in association with a large heart. Riesenfeld [8] reported five cases of cardiac enlargement with lymphocytic infiltration in the myocardium, all of which were associated with status lymphaticus. Because of the round cell infiltration in the myocardium, Ceelen [1] concluded from his pathologic studies that there is a relationship between the cardiac enlargement and the status lymphaticus. Blühdorn [2] also reported a case of this type and diagnosed it as idiopathic hypertrophy of the heart. It seems to us, therefore, that there is a likely association between the so-called idiopathic hypertrophy of the heart with lymphocytic infiltration in the myocardium and the status lymphaticus, although it must be admitted that cardiac enlargement with myocardial lymphocytic infiltrations may occur in the absence of status lymphaticus. However, the coexistence of true idiopathic cardiac enlargement and status thymicolymphaticus is found only in a few of the cases reported, namely, four of twenty-one cases.

From the clinical standpoint, it is striking to note that in cases of idiopathic cardiac hypertrophy there are surprisingly few clinical manifestations of the extensive changes in the heart which are present until shortly before death. The chief symptoms, which are due to cardiac failure, such as attacks of cyanosis and dyspnea, cough, vomiting and anorexia, occur as already mentioned only shortly before death. On physical examination, the heart may be found enlarged but cardiac murmurs are usually absent. In twenty cases of idiopathic hypertrophy

8. Riesenfeld: Jahrb. f. Kinderh. **86**:419, 1917.

reviewed by Stoloff,[5] systolic murmurs were heard in five; however, these were apparently functional, since autopsy did not reveal any organic cause.

The diagnosis of this condition is one made by exclusion, the history of attacks and the presence of dyspnea, and cyanosis in the absence of signs of pulmonary disease or the usual signs of congenital cardiac disease such as murmurs should be suggestive. Stoloff emphasized the fact that a history of repeated attacks of cyanosis and dyspnea was infrequent in the majority of cases he reviewed, and that other suggestive symptoms were absent until shortly before death.

SUMMARY

A case of true idiopathic cardiac enlargement associated with status thymicolymphaticus is reported.

No lymphocytic infiltration in the myocardium could be demonstrated.

The case illustrates the clinical picture of sudden onset with rapid fatal termination.

A review of the literature reveals twenty-one cases of true idiopathic hypertrophy, including the case presented here. In four (19 per cent) of these cases, there was an associated status thymicolymphaticus. Seven other cases reported as so-called idiopathic hypertrophy showed lymphocytic infiltrations into the myocardium, in six of which there was an associated status thymicolymphaticus.

No definite relationship could be established between idiopathic enlargement of the heart and status thymicolymphaticus with or without lymphocytic infiltration of the myocardium.

ACUTE BACTERIAL ENDOCARDITIS IN INFANCY

A REVIEW OF THE LITERATURE AND REPORT OF A CASE IN A FIVE WEEKS OLD INFANT *

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AND
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To the pediatrician, infantile endocarditis is considered a rare condition, its rarity being reflected in the views of various observers. According to Finkelstein,[1] "Endocarditis is so extraordinarily seldom seen that it would seem that the endocardium of the infant is possessed of definite immunity." Morse [2] contended that acute endocarditis seldom if ever develops during the first three years of life. Still [3] said: "The possibility of acquired simple endocarditis in a child under two years of age can be almost excluded on account of the fact that simple endocarditis almost invariably follows articular rheumatism which hardly ever occurs under three years of age and almost never under two."

REVIEW OF THE LITERATURE

After reviewing the literature, we are inclined to weigh with considerable merit the views of the aforementioned observers, as we were able to find only five cases in infants under 7 months of age.

The case of the youngest patient was reported by Blum.[4] There was a pyocyaneous septicemia with a complicated endocarditis in a child aged 2½ months. The infant was also affected with papular syphilid.

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* Submitted for publication, Dec. 14, 1929.

* From the Departments of Pediatrics and Pathology, the University of Minnesota.

1. Finkelstein, H.: Lehrbüch des Säuglingskrankheiten, Berlin, H. Kornfeld, 1905.

2. Morse, J. H.: Clinical Pediatrics, Philadelphia, W. B. Saunders Company, 1926.

3. Still, G. F.: Common Disorders of Diseases of Children, London, H. Frowde, 1915.

4. Blum, S.: Centralbl. f. Bakteriol. u. Parasitenk. **25**:113, 1899.

Lempp [5] reported seven cases from Finkelstein's clinic. All of the cases occurred in infants, the youngest being about 4 months. The mitral valve was shown by autopsy to be involved in every case.

Of forty-five cases in children, Steffen [6] observed five cases in infants under 1 year of age.

Still [3] stated that he had seen two cases of malignant endocarditis, one in a child of 7 months and another in a child of 2 years, both cases being associated with empyema.

Skinner [7] cited a case that occurred in an infant of 4 months. At autopsy the mitral valve was found to be extensively covered by a growth of soft vegetations.

Dible [8] mentioned a case of streptococcal endocarditis of the aortic valves in an infant of 6 months. The other valves of the heart were normal. The kidneys showed numerous well marked miliary infarcts of recent date.

In a series of forty-five cases, Von Dusch [9] observed five cases in infants between the ages of 8 months and 3 years.

Dean [10] reported a case of ulcerative endocarditis in a child of 3 years, which was due to the pneumococcus. In his case, the mitral and tricuspid valves were affected.

Bass [11] quoted a case that occurred in the first month of life, as reported by Czerny. In reviewing the literature carefully, no evidence has been found to substantiate this report.

In 1,000 autopsies, Holt [12] found no case of acute endocarditis in children under 3 years of age. His youngest patient was a boy of 4, in whom the condition was on the right side. Most of his patients were over 10 years of age.

REPORT OF CASE

We are presenting a case in an infant of 5 weeks. This, we think, is the first authentic case occurring within the first six weeks of life to be reported.

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5. Lempp, K.: Monatschr. f. Kinderh. **6**:78, 1907.

6. Steffen, A.: Klinik der Kinderkrankheiten, Berlin, A. Hirschwald, 1889, vol. 3.

7. Skinner, E. F.; Lancet **1**:1147, 1922.

8. Dible, J. H.: J. Path. & Bact. **23**:196, 1920.

9. Von Dusch, T., in Berhardt: Handbuch der Kinderkrankheiten, Tübingen, 1878, vol 4, p. 324.

10. Dean, H. R.: Brit. J. Child. Dis. **9**:317, 1912.

11. Bass, M. H., in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1924, vol. 4, p. 362.

12. Holt, L. E., and Howland, J.: Diseases of Infancy and Childhood, New York, D. Appleton & Company, 1926.

History.—A white boy was born at Ancker Hospital in St. Paul on Dec. 9, 1928, at full term; the delivery was normal. Physical examination gave negative results at birth. The infant left the hospital on December 19. Soon after that, the mother became ill with a grippal infection, and, as she was unable to care properly for the infant, he was put into a private home.

Examination.—On Jan. 2, 1929, examination showed an apparently normal infant. There was no evidence of influenza, notwithstanding a clear history of exposure. The infant was artificially fed and progressed nicely until January 11

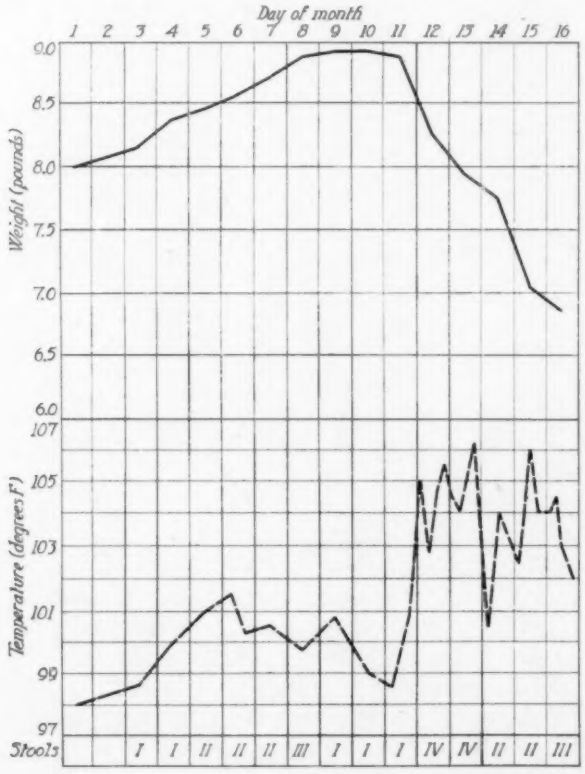

Fig. 1.—Chart showing the sudden onset and course of the illness.

(he gained 14½ ounces [411.07 Gm.] in nine days). On that day, the temperature rose suddenly to 105 F. (rectal); there was marked loss in weight; the stools became frequent and loose, and the infant appeared listless, with marked clouding of the sensorium. The results of physical examination were otherwise negative. The condition was then considered a possible toxicosis, and the proper treatment was instituted, with no response (fig. 1). The infant took feedings well, notwithstanding his septic condition.

The following day, examination showed fine crepitant râles over the base of the right lung posteriorly. The heart presented no abnormal sounds and was considered apparently normal. The septic, listless state seemed more pronounced,

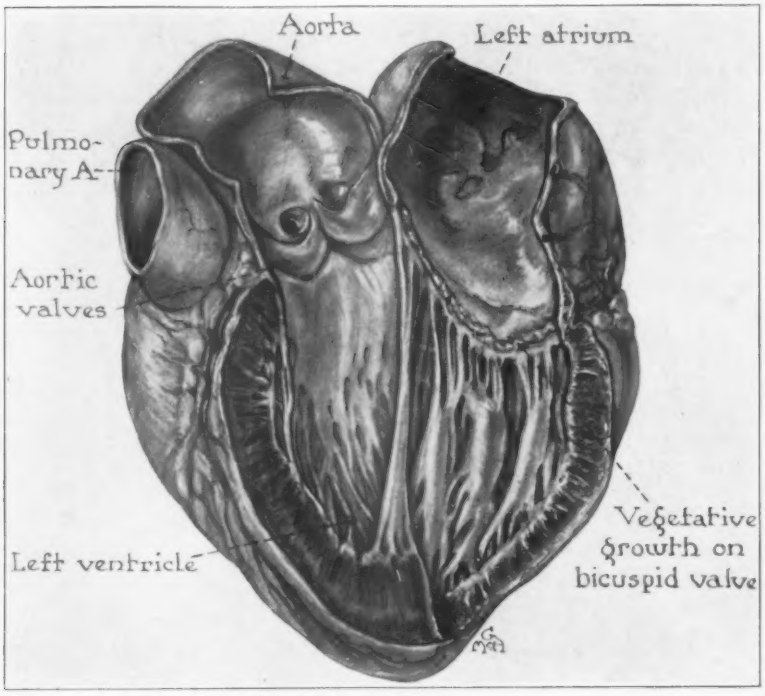

Fig. 2.—Drawing, showing the extent of valvular involvement.

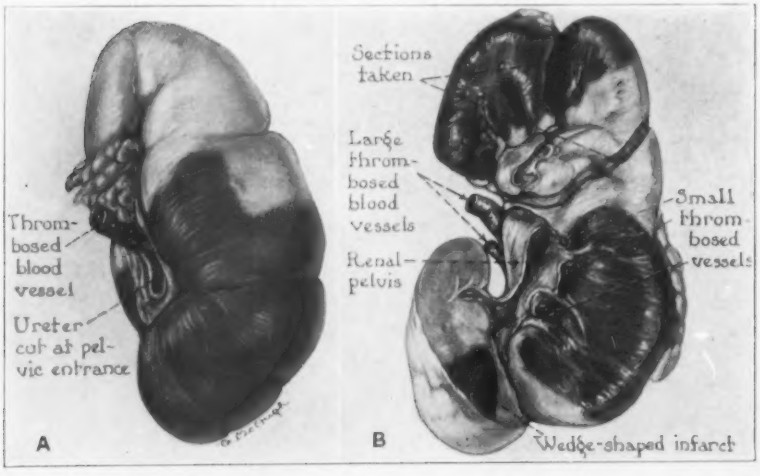

Fig. 3.—*A*, drawing of the anterior surface of the left kidney, showing the occlusion of the vein, with involvement of the entire lower half. *B*, the posterior half of the right kidney exposed, showing the extent of the infarcted areas.

and the infant had a series of short convulsions, accompanied by marked pallor, twitchings of the muscles of the face, rolling of the eyes and general rigidity of the body, with slight bulging of the anterior fontanel. Chloral hydrate, 7½ grains (0.784 Gm.), was administered by rectum, and the convulsions did not recur. The fever, loss of weight and listlessness persisted until January 16, when the infant died (five days after the onset of illness).

Autopsy Report.—Gross Pathology: The body was that of a rather poorly developed and poorly nourished boy, 52 cm. in length weighing about 7 pounds (3,175.14 Gm.). The abdomen was distended and tympanic; the lips were cracked and covered with a foamy, bloody exudate. The skin was excoriated over the buttocks; rigor was present. There was questionable edema of the feet. No evidence of jaundice was present. The pupils were dilated, regular and equal.

When the abdominal cavity was opened, no abnormalities were present except a small amount of gaseous distention of the bowels.

The pericardial sac contained 5 cc. of a clear fluid. Its surfaces were smooth and nonadherent.

The heart weighed 19 Gm., with the foramen ovale closed. The myocardium was dark red and firm. All the valves, except the mitral, were normal. On the auricular surface of the latter there was a line of minute, firm, pale nodules, variable in size but averaging 1 mm. in thickness. They were approximately 2 mm. from the free margin of the valve. The ventricular and auricular myocardium was normal (fig. 2).

The right lung weighed 46 Gm. There were several small areas of fibrinopurulent pleurisy on the lower lobes of both lungs. Crepitation was normal except in a few small areas at the bases of both lungs, where it was reduced. On section of the latter areas, an excess of frothy fluid and occasional droplets of pus were expressed.

Each kidney weighed 14 Gm. The lower half of the left kidney and the upper and lower fourths of the right kidney were dark and hemorrhagic, due to infarcts. The infarcted areas were slightly swollen, and on cut section no blood oozed from the surface. The rest of the kidneys, including the pelves and ureters, appeared normal (fig. 3).

The spleen weighed 11 Gm. It was dark red and firm and appeared normal both externally and on cut section. The weight of the liver was 121 Gm. No abnormalities were present. The gallbladder and its ducts, the pancreas and the suprarenal glands were normal. The thymus weighed 2.5 Gm.; no changes were evident. No adenopathy was present.

Microscopic Pathology: There was diffuse bronchopneumonia of the lower lobes of both lungs. The remainder of the tissue of the lungs was normal.

The spleen, pancreas and suprarenal glands were normal.

The myocardium showed no Aschoff nodules. Unfortunately, no section was made of the affected valve of the heart.

The interstitial substance and tubular lumina of the kidney contained considerable hemorrhage. The glomeruli were all practically free from excess red blood cells. Most of the tubular epithelium in the hemorrhagic areas was necrotic, while that outside the infarct was of normal appearance. The interlobar veins corresponding to the infarcted areas were completely occluded by fairly recent thrombi. This occlusion extended into all the smaller tributaries. No occlusion was evident in any of the corresponding arteries (figs. 4 and 5).

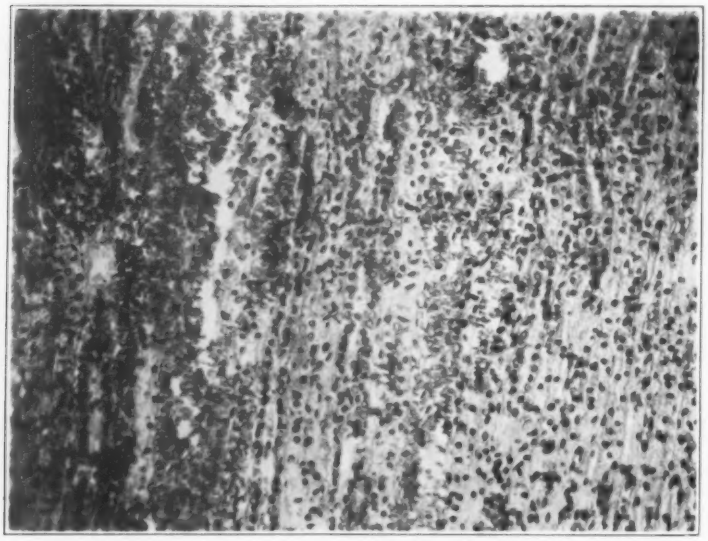

Fig. 4.—Photomicrograph, showing the necrotic tubules in the hemorrhagic areas.

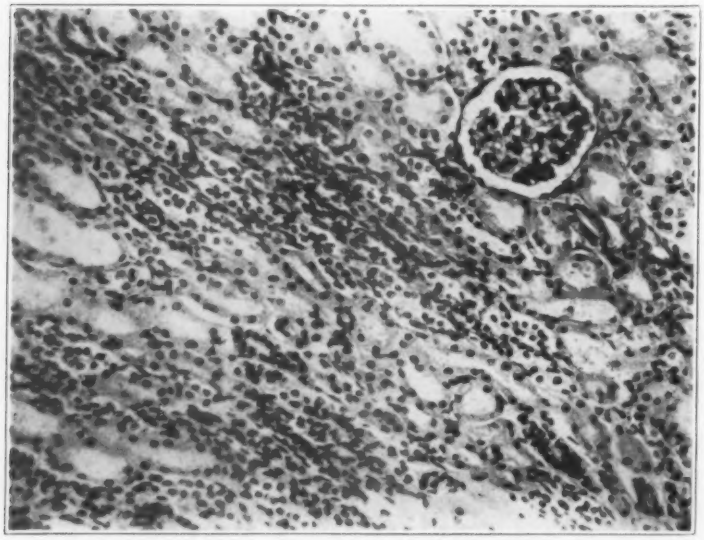

Fig. 5.—Photomicrograph, showing the glomeruli free from excess red blood cells.

COMMENT

This case again illustrates the difficulties encountered in the varied diagnostic problems. Here the exact pathologic condition was unrecognized until autopsy clarified the condition.

The sudden onset with fever, rapid loss in weight, frequent stools and dulled sensorium simulated very much a beginning toxicosis. Proper treatment was immediately instituted, with no results. The septic nature of the infant could not be entirely attributed to the small pathologic changes in the lungs. We were never able to detect a murmur of the heart. No explanation could be given for the rapid progressive loss in weight nor for the septic temperature.

We are at a loss to explain the etiology of the existing endocarditis. The question as to its relation to a grippal infection [1] contracted from the mother might have some bearing in this case.

The involvement of the kidney was marked. It was considered that the venous thrombosis was caused by a phlebitis of the renal veins secondary to the endocarditis and pneumonia. As a result of this venous occlusion, a hemorrhagic infarct resulted in the renal tissue drained by the occluded veins.

THE DANGER OF MOUTH-TO-MOUTH BREATHING IN RESUSCITATION OF THE NEW-BORN INFANT*

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ST. LOUIS

Of the various modes of resuscitating an asphyxiated new-born infant, direct mouth-to-mouth insufflation of the lungs enjoys great popularity among practitioners. Although it is probably the easiest and quickest method of filling the collapsed lungs of the child with air, the danger of rupturing the delicate alveoli by too much force, and of producing a pneumothorax is considerable. For this reason many authors either warn against its use altogether or sponsor it only if most painstaking precautions are observed.

How well founded their objections are may be seen from the following case.

REPORT OF CASE

A sextipara, aged 42, near term, was admitted to the hospital with profuse bleeding. The cause of the bleeding was a placenta praevia centralis, and as the case was further complicated by a transverse position of the fetus, cesarean section was decided on and performed by the chief of the department, Dr. George Gellhorn. The infant, a boy, apparently a little below the average weight, was extracted and handed over to an intern, who attended to the care of the umbilical cord in an adjoining room. Presently, there was a weak cry, and the infant was taken to the nursery on another floor of the building. After the completion of the operation, the nurse in charge reported that the infant appeared normal at first, but soon became cyanotic and breathed irregularly. On examination, the color of the skin was found to be deep blue, and the respiration was rapid and shallow. The infant continuously emitted moaning and whining sounds. Only when oxygen was administered and external heat applied did the condition improve a little, but the improvement was of short duration.

The pediatrician on duty, Dr. T. Wistar White, who was notified at once and arrived a few minutes before the infant died, suggested that an x-ray picture be taken. The picture (figure) revealed "a complete atelectasis of the right lung. The left lung was also collapsed and pushed to the midline by a large accumulation of air in the thoracic cavity. A dense triangular shadow in the upper portion of the chest was suggestive of a large thymus. The cardiac shadow did not seem to be enlarged." (Dr. L. R. Sante.)

These observations could be interpreted either as a congenital anomaly such as a pulmonary fistula or as the result of traumatism. Before assuming the former and rather far-fetched possibility, the intern who had taken charge of the

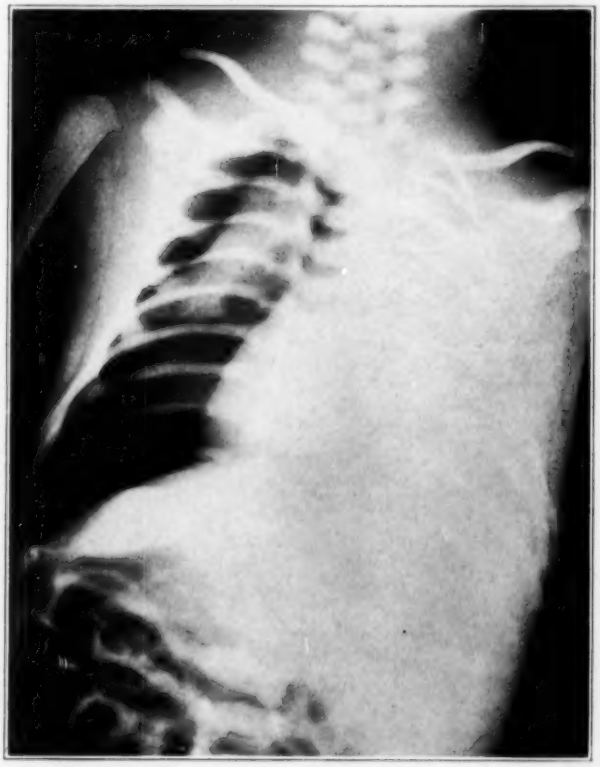
* Submitted for publication, Dec. 24, 1929.

* From the Department of Gynecology and Obstetrics, St. Louis University School of Medicine.

infant immediately after birth, was interviewed. It was then learned that the child had not breathed promptly and that the intern had resorted to mouth-to-mouth breathing which, as he insisted, had been gentle. However gentle his procedure may have been, the artificial pneumothorax proved that the force of direct insufflation had been far too great for the resisting strength of the frail tissues of the lungs.

COMMENT

The loss of life in this case is truly deplorable, and there can be no doubt that it was due to the faulty technic on the part of the intern.



Pneumothorax following mouth to lung breathing in resuscitation of the new-born infant.

On the other hand, it is humanly understandable that a less experienced obstetrician, in the excitement of seeing a life entrusted to his care slip away, may underestimate the extreme delicacy required for mouth-to-mouth breathing. It would be better, therefore, to abandon this method of resuscitation in general practice at least, and supercede it by other less dangerous modes of treatment for asphyxia pallida.

Metropolitan Building.

INFANTILE PULMONARY TUBERCULOSIS DUE TO AN UNUSUAL TYPE OF TUBERCLE BACILLUS *

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Virginia R. was born on Oct. 4, 1927. At birth, she weighed 7¾ pounds (3.5 Kg.). When examined, she was found to be normal in all respects. There was nothing unusual about her progress, except that she was weaned on the third day, and from then on was fed artificially. On discharge from the hospital at the end of the second week of life, she was gaining normally. When seen on November 8, at 5 weeks of age, she was found to have become pale, although her progress in weight had been good. There was some nasal discharge, and she was thought to have a cold. In all probability, these were the symptoms of the illness which was clearly demonstrated at the next visit, when she was 11 weeks of age. She then had a fever and a cough which had been noted three days before; the pallor had increased somewhat. Examination now revealed dulness in the apex of the right lung where there was a large area of bronchial breathing under the right axilla, extending to the nipple line in front and to the scapula posteriorly. There were no râles. A diagnosis of pneumonia was made in spite of the fact that the average temperature was around 101 F.

The clinical condition remained the same for two weeks, at the end of which a roentgen examination was ordered because the degree of dulness and the area involved had increased. The x-ray picture, taken on Jan. 24, 1928, was strongly suggestive of fluid (fig. 1). It showed what seemed to be an extensive consolidation, involving practically the whole lung structure on the right. In places, the density was uniform, and the trachea and the heart were displaced toward the left. Accordingly, thoracentesis was performed. A very small amount of fibrous material was withdrawn, which was sent to the laboratory for study. Cultures and inoculations were made from the aspirated material. A stained smear contained innumerable acid-fast, granular rods. The temperature and other signs in the infant continued about the same. She held her weight, but there was no gain. The cough was troublesome, becoming almost paroxysmal at times, and the child had attacks of choking on the material coughed up. At this point, physical and roentgen examinations of the parents and attendants of this child were negative for tuberculosis. A second picture was taken on Feb. 11, 1928, to determine whether there might be a localized accumulation of fluid (fig. 2). This, however, was not demonstrated. There was a decrease in the dense uniform shadow, and near the apex was an area of rarefaction, which suggested either cavitation or pnemothorax. A smear of the sputum taken at this time showed large quantities of the same bacilli as those obtained from the pleural fluid. A scratch tuberculin test was negative, but 0.1 mg. of old tuberculin given intracutaneously produced a slightly positive reaction.

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* Submitted for publication, Dec. 20, 1929.

* Read, Nov. 9, 1929, at the annual meeting of the Pediatric Society of the University of Michigan, at Ann Arbor; the president's address.

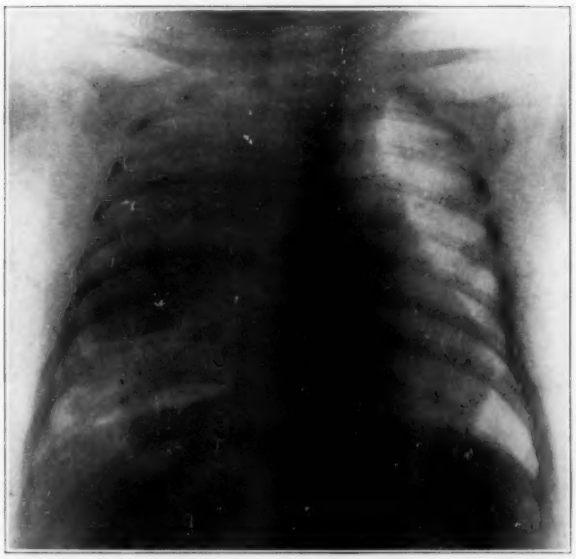

Fig. 1.—Jan. 24, 1928, x-ray picture shows an extensive consolidation involving practically the whole lung structure on the right.

Fig. 2.—Feb. 11, 1928, x-ray picture shows an area of rarefaction near the apex.

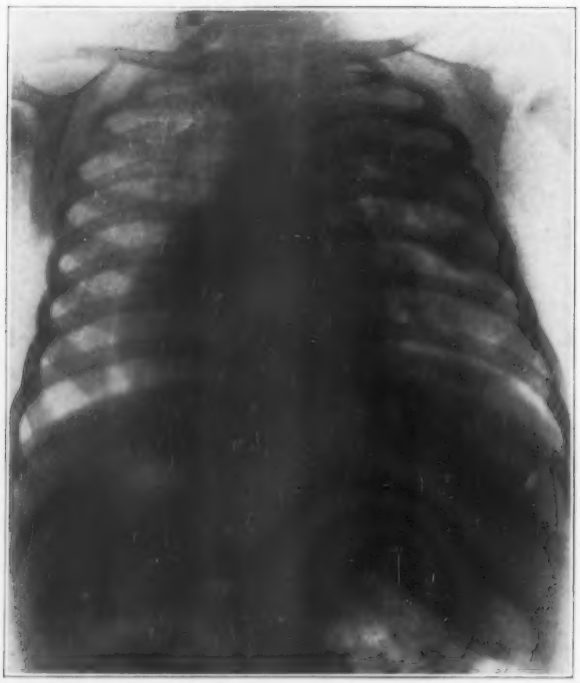

Fig. 3.—March 26, 1928, the dense shadow on the right (fig. 1) has begun to resolve. The process appears on the left.

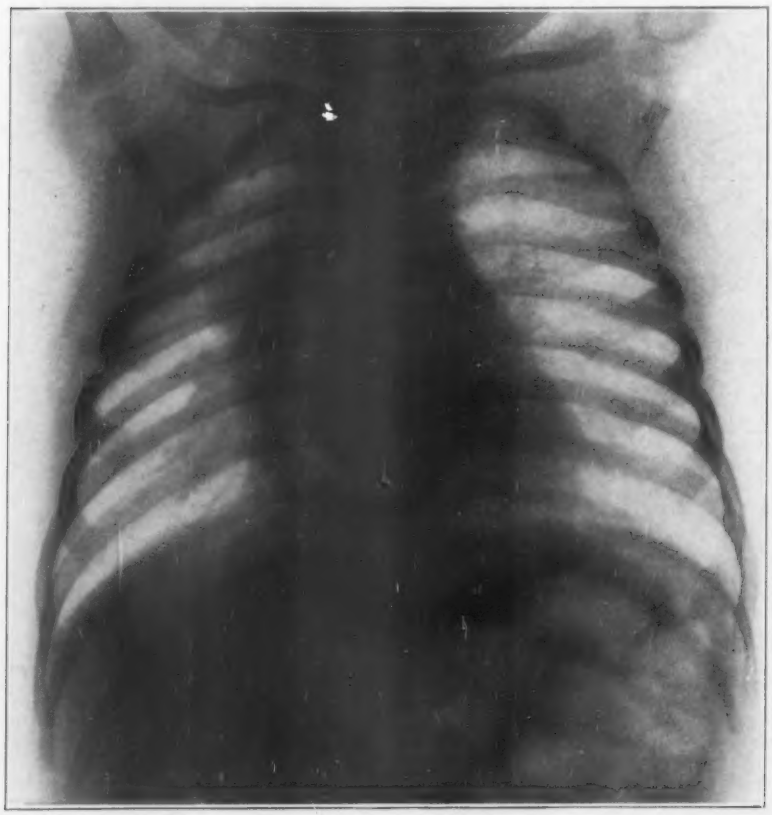

Fig. 4.—Sept. 26, 1928, x-ray picture shows healing of tuberculous process.

From this time on, the fever began to recede, and a slight gain in weight was noted. The cough was still present, but was less frequent and less distressing. The fever did not entirely leave until the patient was 5½ months old. Even at this time, however, the signs in the chest were still marked. There was dulness over the entire right side of the chest, with bronchial breathing and absence of râles. At this time, March 26, 1928, the third picture was taken (fig. 3). The dense shadow now had definitely begun to resolve. While mottling was present throughout the parenchyma, there was definite resolution toward the periphery. For the

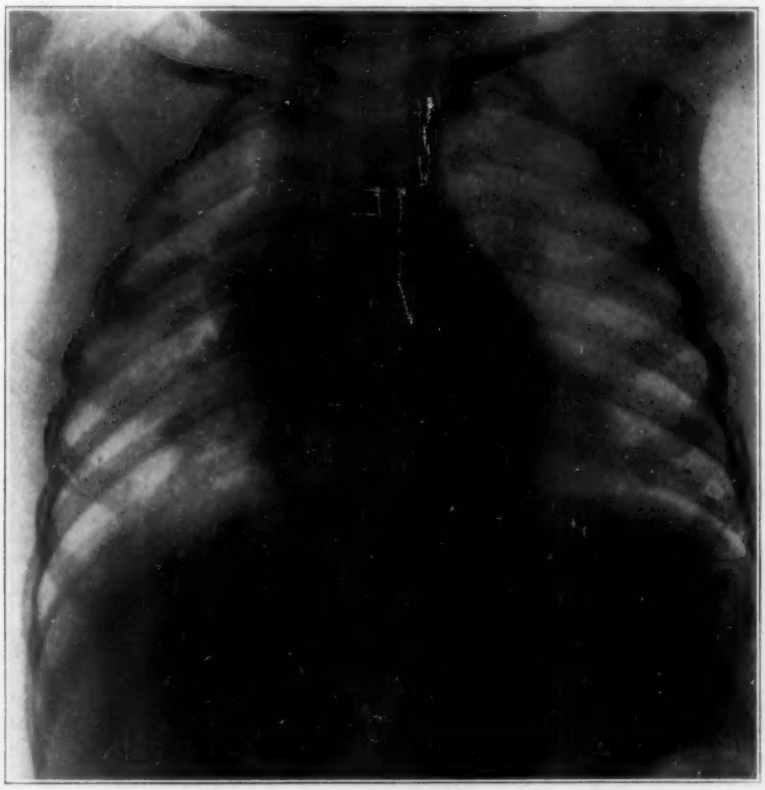

Fig. 5.—May 6, 1929, x-ray picture shows continued healing.

first time, the process appeared on the left, and, while there was no consolidation, there was definite bronchial feathering in the upper lobe. The clinical picture, however, was one of distinct improvement. Alpine light therapy had been begun as soon as the diagnosis of tuberculosis had been made. When the patient was 7½ months of age, or about six and a half months from the beginning of her illness, she weighed 13$^{3}/_{16}$ pounds (5.99 Kg.), and was beginning to sit up. At this time, the cough had entirely ceased, the pallor had about disappeared, and the signs in the chest were confined to an area extending as originally from the nipple anteriorly under the axilla to the angle of the scapula. The x-ray picture taken on Sept. 26, 1928, when she was nearly 1 year of age, is shown in figure 4. For the first time,

the process was shown to be definitely tuberculous. There were signs of healing on both sides, more readily demonstrable on the left, where there was some calcification. On the right, the process had receded from the periphery, so that the lung structures, though mottled, could readily be made out. There was a definite enlargement of the tracheal glands, which almost gave a suggestion of abscess formation within these glands. The child continued to do well, so that at 12 months of age she weighed 20 pounds (9 Kg.) and was beginning to walk with help. The signs were present, but not so marked. An x-ray film taken on May 6,

Fig. 6.—Aug. 2, 1929, x-ray picture shows involvement of lung still present, but no large areas of consolidation.

1929 (fig. 5) when she was 19 months of age, is in the next series. It showed nothing new, except a continuation of the improvement. The last film (fig. 6), taken on Aug. 2, 1929, showed the hilum shadow smaller, and while the involvement of the lung parenchyma was still present, there were no large areas of consolidation. At that time, the patient weighed 25 pounds (11.3 Kg.) and the lung signs had entirely disappeared, except for evidence of the enlargement of the mediastinal glands. With this exception, the child is to all appearances, at present, normal.

LABORATORY REPORT

The nature of the infecting organism in this child's lung was studied by Dr. Bayne-Jones. The smear from the exudate removed by the needle showed numerous long, curved, acid-fast rods. Planted on blood agar plates and incubated aerobically at 37.5 C. for forty-eight hours, these organisms grew in small yellowish-white colonies, pastelike, yielding rods that stained granular by the Gram and Ljubinsky method, and acid-fast by the Ziehl-Neelsen method.

The results of the inoculation in the animals were as follows: Guinea-pig 1, inoculated with direct exudate and killed in seventy-five days, showed no lesions. Guinea-pig 2, inoculated with a small amount of culture and killed in seventy-three days, showed no tuberculosis. Guinea-pig 3, inoculated with 1 cc. of heavy suspension (slant cultures five days old emulsified in 10 cc. of salt solution, a smooth emulsion) and killed in seventy days, showed caseous tuberculosis. The lesions of lymph nodes in the groin at the site of the inoculation were noted. Smears showed acid-fast rods. The organism grew as rapidly and had the same characteristics of colony formation and of morphology as the original cultures. A guinea-pig inoculated with a piece of the caseous gland and killed seven months later showed no lesions.

Two roosters inoculated in the pectoral muscles and subcutaneously with a heavy suspension and killed in seventy days showed no lesions. A rabbit inoculated and killed in seventy days presented caseous lymph nodes at the site of inoculation. There were small, acid-fast rods and granules in the smears. Cultures on glycerin egg mediums (Cooper's method), however, were negative.

Dr. Bayne-Jones sent this unusual organism to Dr. J. D. Aronson, of Phipp's Institute, Philadelphia, who made the following observations: "While it has a somewhat drier and more chalky appearance than the avian, it is certainly more suggestive of that organism, were it not for the rate of growth, and the non-pathogenicity for chickens. It resembles in its appearance the Kedrowsky strain of *Bacillus leprae*."[1] A culture sent to Dr. S. A. Petroff, of Saranac, N. Y., was injected by him into mice, guinea-pigs, chickens and rabbits. All gave negative results, except the rabbit, into which the injection was made intravenously. When, in fifty-five days, it was killed, there were three small foci containing acid-fast granules in the left suprarenal gland. A rabbit into which the organisms were injected intraperitoneally was uninfected.[2]

COMMENT ON LABORATORY REPORTS

I shall refer to a number of reports of cases which clinically resembled the one here reported but in none of which I have been able to find a description of the bacillus causing the infection. The general opinion is that the human and bovine types are pathogenic for man, but that the avian is not. Thus, the English commission for the study of tuberculosis[3] recognized only these two types of tubercle bacilli as

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1. Aronson, J. D.: Personal communication to the author.

2. Petroff, S. A.: Personal communication to the author.

3. Flick, F. L.: Development of Our Knowledge of Tuberculosis, Philadelphia, p. 739.

pathogenic. Baldwin and Petroff [4] concluded that: "The question of the possibility of the avian type infections in man requires study, since cases of renal tuberculosis have been attributed to this type. Until further evidence has been produced, the danger from avian type infection may be left an open question and of but slight importance." But more recently, L'Esperance [5] showed what she believed to be evidence that avian bacilli may be the cause of Hodgkins' disease in man. She felt that her observations justified the conclusion that in the chickens which she inoculated with Hodgkin's glands, there were lesions with the histologic features of Hodgkin's granuloma and comparable with avian tuberculosis. This introduces the strong possibility of the pathogenicity of the avian bacillus for man. She further demonstrated that while the avian bacilli are nonpathogenic for the usual laboratory animals, except the chicken and the rabbit, they become so, if first dead human or bovine bacilli are injected. As she concluded, "The results obtained in this series of experiments seem to indicate that it is possible to transform an animal relatively resistant to the avian tubercle bacillus into a more or less susceptible one, by previous treatment with a dead heterologous strain of tubercle bacillus." [5] It is clear that the human and bovine strains of the tubercle bacillus are pathogenic. The work referred to may indicate that the avian may become so if the bovine or the human bacillus has rendered the animal sensitive. In this child there was a positive tuberculin reaction showing the child sensitive to the human strain. The organism isolated was shown to be only mildly virulent in animals easily susceptible to human tuberculosis, but in this sensitive child it was pathogenic enough to produce the pulmonary changes described. This organism, then, may be one of a group with the avian bacillus, becoming virulent when it is associated with the human or the bovine tubercle bacillus.

COMMENT ON CASE REPORT

Hempelman,[6] in 1917, called attention to the fact that the prognosis in all infantile pulmonary tuberculosis, even when massive and infiltrating, was not necessarily fatal. He cited a large number of cases, six in patients under 1 year of age. The youngest was only 6 weeks old. All the patients presented what he considered to be massive pulmonary tuberculosis, which was followed by clinical health in each case, the patients being observed for from fifteen months to five years. In one case, that of a 6 months old boy, he recorded the finding of tubercle

4. Baldwin, E. R., and Petroff, S. A.: Tuberculosis, Philadelphia, Lea & Febiger, 1929.

5. L'Esperance, E. S.: J. Immunol. **16**:1, 1929.

6. Hempelman, T. C.: Am. Rev. Tuberc. **1**:99 (April) 1917.

bacilli. Three years later, Eliasberg and Neuland [7] also described the condition which is illustrated here. They found young infants who had positive tuberculin reactions, extensive areas of dulness in the chest, bronchial breathing without râles and mildness of symptoms out of proportion to the signs found. The disease ran a prolonged and benign course, and the infiltration gradually underwent resolution. Since they could find no tubercle bacilli, they called this an epituberculous infection. Langer,[8] two years later, refuted the position taken by these observers and said that he believed the whole process was tuberculous, though of an unusual nature. He demonstrated the tuberculous nature of the process by intensifying the symptoms and signs by injection of tuberculin. The assumption that the whole disease was tuberculous in origin has generally been made by the later observers. Ribadeau-Dumas and BeClere [9] reported the case of a 9 months old infant infected by a servant with open pulmonary tuberculosis. This child had absolute dulness and feeble respiration over the entire right side of the chest. The tuberculin test was positive. When seen in the sixth year, the child was well and strong, and the chest showed no abnormal condition. Eichelberg [10] followed the case of a boy, 13 months old, who had a positive skin test. He was dyspneic and hoarse. An x-ray picture showed a dense shadow over the whole right side of the chest. At 21 months, the child was clinically well, and the x-ray picture revealed the improved condition. Gerstenberger and Burhans [11] reported the cases of seven infants ranging in age from 2 to 17 months, who made uniformly good recoveries. All of these cases were clinically and from a laboratory point of view, similar to those referred to previously. The patients were treated with ultraviolet light. In a similar case, Kohen [12] treated a 12 weeks old infant with ultraviolet light. The child regained normal health. He followed it up for five years. In this group of cases of infantile pulmonary tuberculosis and so-called epituberculosis, there was one thing in common. In each there was a positive reaction to human tuberculin. It is probable that the whole clinical picture in most of them was due to infection with the human tubercle bacillus. It is possible, however, that some of these may have been similar to

7. Eliasberg, H., and Neuland, W.: Jahrb. f. Kinderh. **94**:102, 1921.

8. Langer, H.: Ztschr. f. Kinderh. **34**:143, 1923.

9. Ribadeau-Dumas, M. M., and BeClere, H.: Abstr., Arch. de méd. enf. **23**: 728, 1920.

10. Eichelberg: Monatschr. f. Kinderh. **18**:123 (May) 1920.

11. Gerstenberger, H. J., and Burhans, C. W.: Treatment of Extensive Pulmonary Tuberculosis in Infants with Ultraviolet Rays, Am. J. Dis. Child. **33**:54 (Jan.) 1927.

12. Kohen, J. L.: Amer. Rev. Tuberc. **17**:565, 1928.

the case I describe, and that the chief infection was not with the human tubercle bacillus, but with another organism, morphologically indistinguishable from it.

SUMMARY

There is evidence that while unusual, recovery in an infant with pulmonary tuberculosis is by no means unknown. In reviewing reports of cases, however, I have been unable to discover any reference to the types of tubercle bacilli found. It is possible that nearly all such children had been infected with the human strain of the organism, since they gave a positive reaction in the skin test with that bacillus. But that the destructive agent was that organism may be a wrong assumption. In the case here presented, the organism was morphologically similar to the human tubercle bacillus, but was apparently of an entirely different strain. It may be, therefore, that some infants who recover are infected with an organism similar to the one here reported. Its pathogenicity in the human subject may be related, as L'Esperance's work seems to indicate, to the sensitivity produced by a previous invasion of the human strain of the organism.

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Progress in Pediatrics

THE USE OF BRACES IN OBSTETRIC BRACHIAL PARALYSIS

WITH A REPORT OF TWO HUNDRED AND ELEVEN CASES IN TWO HUNDRED PATIENTS

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NEW YORK

The subject of obstetric brachial paralysis, which up to a few years ago was considered incurable, has been brought before the medical profession by Taylor, Sever, Fairbank,[1] Platt[2] and myself. The etiology has been cleared up. The condition is now considered curable, and the earlier the treatments are instituted, the better are the results. The orthopedic surgeon is now being consulted very early, and thus he has a chance to prevent the distressing and disabling deformities and frequently to institute a complete cure.

The best way of preventing the deformities is still an unsettled question. Some surgeons resort to the use of braces; others depend on massage and exercises alone.

I advocate the use of braces very early in these cases, and I submit herewith a review of the cases of the first 200 patients with obstetric brachial paralysis coming under my care.[3] No attempt was made to use control cases. To give some basis for comparison, however, a considerable number of this group came to me after having been subjected to massage and exercises without the use of braces.

A short review of facts known about this condition and the description of the braces used will not be amiss. The shortcomings of the braces will be discussed. The statistics and results will follow.

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1. Fairbank, H. A. T.: Birth Palsy—Subluxation of the Shoulder Joint in Infants and Young Children, Lancet **1**:1217 (May 3) 1913; Discussion, J. Orthop. Surg. **2**:284, 1920.

2. Platt, H.: Birth Paralysis, J. Orthop. Surg. **2**:272 (May) 1920.

3. These are the first 200 patients whose records I kept.

FACTS KNOWN ABOUT ETIOLOGY AND DEFORMITY

The majority of observers agree with the "traction theory" so conclusively proved by the excellent work of Taylor [4] and afterward corroborated by Sever.[5]

According to the "traction theory," the damage is done by the stretching of nerves of the brachial plexus, by forcible separation of the head from the shoulder during delivery or by direct traction on the arm. The stretching, of course, may often result in complete tear of the nerve fibers. It is almost always associated with difficult labor, forceps being used in many instances.

In untreated patients, usually the arm is kept in adduction and internal rotation with slightly flexed elbow, forearm pronated and wrist flexed. The deformities are, of course, due to contraction of the good muscles, which are unopposed by the weak muscles.

TREATMENT

Treatment with Braces.—As many of these cases are due to stretching of the nerves rather than to actual tearing, and as a great deal of the disability in later life is due to secondary deformities rather than to paralysis, orthopedic surgeons, notably Sever, Fairbanks, Platt and myself, advise early resort to orthopedic treatments. The conclusion was that it is best to have the arm placed as comfortably as possible in such a position that the stronger muscles cannot become contracted. Hence the arm should be placed in a plaster cast or brace, the shoulder abducted and rotated outwardly, the forearm supinated, the elbow flexed and the wrist dorsiflexed.

The reasons for the braces are obvious. Besides preventing the deformities and relaxing the stretched nerves, the brace also takes the drag off the paralyzed shoulder muscles, particularly the deltoid, allowing them to regain their strength more quickly and preventing subsequent deformity of the shoulder, such as subluxation and acromial hooking and overgrowth.

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4. Taylor, Alfred S.: Brachial Birth Palsy and Injuries of Similar Type in Adults, Surg. Gynec. Obst. **30**:494 (May) 1920. Clarke, Taylor and Prout: A Study of Brachial Birth Palsy, Am. J. M. Sc. **130**:670 (Oct.) 1905.

5. Sever, James W.: Obstetric Paralysis, Am. J. Dis. Child. **12**:541 (Dec.) 1916. The Operative Correction of Longstanding Erb's Palsy, Am. J. Surg. **35**: 287 (Sept.) 1921; Obstetric Paralysis: Report of Eleven Hundred Cases, J. A. M. A. **85**:1866 (Dec. 12) 1925.

In previous articles,[6] I have encouraged the use of the shoulder brace, and suggested that the earlier the support is put on, even in the first week, the better is the result (figs. 1, 2 and 3).

As my interest in the cases grew, I found that while the deltoid brace took care of the wrist drop to some extent, frequently the shoulder was cured entirely while the wrist was still weak and had a tendency to show wrist drop. In those cases, I then had to resort to a small cock-up splint. As my study progressed, I found that more and more children needed the addition of a cock-up splint. This finally led me to use the cock-up splint together with the deltoid in every case in which there was any weakness of the wrist muscles.

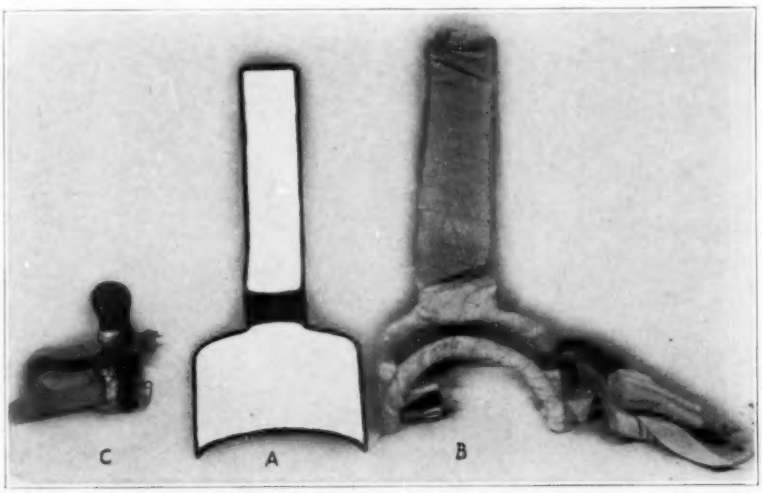

Fig. 1.—Simple deltoid and cock-up splints, anteroposterior view. *A*, wire deltoid splint before padding; *B*, deltoid splint padded with straps; *C*, cock-up splints made of duralite.

Of course, both braces are disposed of gradually; at first for a few hours a day, then for the greater part of the day, and then all day. Finally the brace is left off altogether.

Use of Massage and Muscle Training.—Massage and exercises are of the greatest importance and should be given daily if possible. If a child is brought to me within a week of birth, I apply the braces and leave them on for five days undisturbed. If the shoulder is still tender,

6. Boorstein, Samuel W.: Obstetric Paralysis (Erb's Palsy), with a Report of Seventeen Cases, Med. Rec. **96**:790 (Nov. 15) 1919; Treatment of Obstetric Brachial Paralysis, with a Report of Fifty Cases, J. Bone & Joint Surg. **5**:778 (Oct.) 1923; Obstetric Brachial Paralysis (Erb's Palsy), J. A. M. A. **82**:862 (March 15) 1924; Birth Injuries Requiring Orthopedic Treatments, ibid. **85**:1866 (Dec. 12) 1925.

I leave it on for five days longer and then begin the massage. The braces are taken off for massage and gymnastic treatments, but are reapplied immediately.

The massage should be administered very gently and then followed by exercises. It is most unwise to allow a child to become obsessed with the idea that it has an arm that cannot be used. Exercises should consist of stimulating movements in the arm produced by games and by reaching for toys, efforts being made to encourage voluntary movements of the affected member. In the Boston Children's Hospital, rimes and songs have been instituted to obtain voluntary response from the infants.

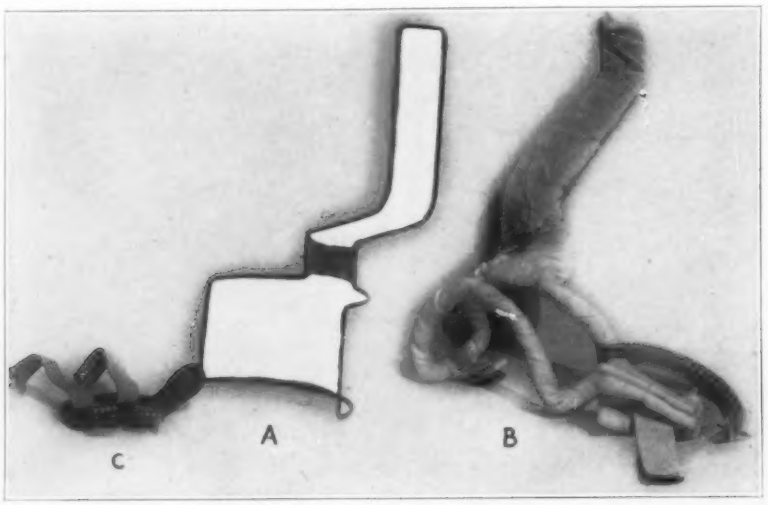

Fig. 2.—Simple deltoid and cock-up splints, lateral view. *A*, wire deltoid splint before padding; *B*, deltoid splint padded with straps, showing the hyperextension of the wrist; *C*, cock-up splints made of duralite.

When the child becomes older, it is possible to carry out the exercises more effectively, adding at the same time games, the use of dumb-bells, etc.

Other or Later Treatments.—I think that if these patients are treated early and properly, one may expect good recovery within three or four months in the mild cases. The more severe cases will require about six or seven months for complete recovery. If contractures develop in the subscapularis and pectoralis major muscles, or if the child comes under observation after the deformities have already developed, the deformities must be corrected before any treatment is attempted. The discussion of these operations is beyond the scope of this article. In many cases, particularly those of the upper arm

type, there will be perfect recovery when these orthopedic conservative treatments are given, and no operation will be necessary. In some cases of upper and in a great many of the lower type, an operation has to be undertaken on the plexus to repair the damage.

OBJECTIONS TO THE USE OF BRACES

There are some surgeons who raise objections to the use of braces in these cases. Their chief claims are: (1) The brace is uncomfortable;

Fig. 3 (case 196).—A double Erb's, showing the position of the left arm, adduction and internal rotation. The right hand has the deltoid brace, showing how simple it is to apply. It can be used over the clothing.

(2) it causes atrophy; (3) it causes stiffness at the shoulder, and (4) it is of no benefit, as proper massage and exercises will give the same results.

The first objection can easily be answered, as these braces can be applied in such a manner as to be very comfortable and cause no pressure. As a matter of fact, infants who cry when the arm is handled frequently stop crying when the brace is put on.

The second objection, that of atrophy, is offset by the massage and exercises which are applied.

Stiffness of the shoulder is a real objection, and in a few of my cases there was some stiffness, but as soon as the brace was dispensed with and the exercises were performed more frequently, the adhesions were loosened (figs. 4 and 5). One has to be careful from the beginning, however, not to keep the brace on too long, so that adhesions

Fig. 4 (case 2).—Alvin A. on Feb. 1, 1923, aged 2 years and 2 months, showing how much the right arm can be abducted. The shape of the deltoid shows that there were some adhesions at the capsule.

Fig. 5 (case 2).—Alvin A. in March, 1929, aged 8 years and 4 months. The figure on the left shows the power of abduction and outward rotation. The figure on the right shows the slight limitation to supination, but the patient wrote with the hand and used it freely.

will not occur. This is particularly true in cases in which there is some injury to the capsule of the shoulder as evidenced by tenderness (case 2).

It is easier, however, to loosen the adhesions that occur when the arm is abducted than those which occur when the arm is not supported by a brace and which finally lead to the typical deformities of adduction, inward rotation, etc. The latter condition requires open operation.

The fourth objection, that the brace is of no real benefit, led me to study the first 200 consecutive patients who came under my care, and to get the end-results when possible. All of the patients who came to me early received braces. There were among the group patients who were brought to me at the age of 3 months and up, on whom braces had not been used. These cases afforded me some opportunity for comparison.

The accompanying table gives an analysis of the cases of 200 patients (211 cases).

COMPARISON OF USE AND NONUSE OF BRACES

Referring to the results in the table, one can see that of those patients who were treated by braces very early and who came for treatments regularly, 97 made a good recovery. Of those who were not treated by braces and consulted me later, 47 still had a great deal of paralysis at that time, as shown in the table. Many of these patients have improved rapidly with the use of braces even though this device was resorted to later.

The principle of the braces in obstetric paralysis is the same as in anterior poliomyelitis and peripheral nerve injury. Just as in these two diseases the progressive orthopedic surgeon does not hesitate to put on a brace immediately, so in obstetric brachial paralysis he should resort to it at once.

It is true that there are cases of mild paralysis at birth that clear up spontaneously in a few days or weeks. However, correct relaxation of the affected parts by splinting will lead to more rapid recovery, while if the paralysis is of a more serious nature, the sooner the treatment is started, the better are the results. The brace is applied to infants 1 or 2 days old. Should the condition prove to be temporary, no harm has been done, and the infant should recover more quickly. If the paralysis is more serious, the correct treatment has been started at once, and the injury to the nerves may be prevented from increasing in extent, especially when one has to keep in mind that in many instances the nerves are only stretched and not actually torn.

The application of the braces is so easy that the general practitioner should become conversant with it. One has to remember mainly that the arm is to be in abduction (at a right angle with the torso), rotated outward, the elbow flexed at a right angle, with the palm facing the face. If there is weakness of the wrist, a small contrivance (a cock-up

splint) to have the hand in slight hyperextension should be added (figs. 1*C* and 2*C*).

When one sees the large percentage of excellent and good results (table) when patients are treated early, the value of the brace is self-evident.

It may be true that some of the patients might have been cured without any treatment, but, as stated before, nothing was lost by early treatment. It is of course doubtful whether such a big proportion would have been cured. The results in anterior poliomyelitis prove this.

PRECAUTIONS NECESSARY

The precautions necessary are: The brace should not press in at the axilla; it should not be too short at the forearm, and it should not be left on too long, as it may cause stiffness of the shoulder or elbow. By removing the braces for massage and manipulating these joints carefully, no stiffness occurs.

REPORT OF CASES

CASE 1 (series 1).—Herbert A. was 3 weeks of age when referred to me by Dr. Ballen in 1918. He had paralysis of the entire right arm. There was a distinct history of difficult labor followed by the use of forceps. A plaster cast was applied and left on for ten days, when it was opened and made into a removable splint. Baking, massage and muscle training were begun; the plaster splint was taken off only for the massage. After five months, the support was left on only at night. The child made a good recovery in five months, but was kept under observation for two years. The only deficiency of function was that of supination. The child could supinate only to about three fourths of normal. At the time this article was written, however, he had good use of the entire limb; he could even play the violin (fig. 6). I advised an operation on the pronator radii teres, but the parents refused.

Comment.—Thus, a child who would probably have had permanent paralysis of the lower type regained almost full function because the limb was kept in proper support, which guarded mainly against deformities and prevented undue stretching of the denervated muscles, while regeneration of the nerves was facilitated by massage and exercises. No electricity was used. The only deficient function is the supination. In later cases, I stopped using plaster, as it is uncomfortable for the child. I resorted to the use of braces which were removed at an early age.

CASE 2 (series 27).—Alvin A., aged 4 weeks, when referred by Dr. Rubinstein, had paralysis of the entire right arm. There was a distinct history of impacted shoulder. The child was put in a plaster cast for two and a half weeks, and then the usual treatments were instituted. After treating the child for two months, I found that he kept the arm continually in an abducted position (about 90 degrees with the torso) owing to adhesions that had formed. It took about four months

Statistics Concerning the 211 Cases in the 200 Patients Seen Consecutively by Me

Sex

Male	110
Female	90
Total	200

Side Affected

Right	121
Left	68
Both	11
Total	200

Presentation

Vertex	153
Breech	41
Not known	6
Total	200

History of Labor

Normal delivery	68
Difficult labor (but no forceps used)	54
Forceps	69
Undetermined	9
Total	200

Another member in family with similar condition..... 3
(Occurred in three families and I saw all six cases)

Position of Affected Child in Family

First	67	Eighth	2
Second	56	Ninth	1
Third	29	Tenth	1
Fourth	15	Eleventh	1
Fifth	14	Sixteenth	1
Sixth	5	Undetermined	5
Seventh	3		
Total	200		

Age When First Seen by Me

First week	43	Sixth year	4
Second week	25	Seventh year	3
Third week	15	Eighth year	4
Fourth week	9—92*	Ninth year	2
Second month	27	Tenth year	2
Third month	9	Eleventh year	1
Fourth to sixth month	11	Twelfth year	1
Sixth month to one year	7	Thirteenth year	2
Second year	16	Fourteenth year	2
Third year	5	Sixteenth year	1
Fourth year	4	Seventeenth year	1
Fifth year	6		
Total	200		

Type at the Beginning †

Upper	72
Lower	117
Both lower	10
One upper and one lower	1
Total	200

Type at Time of First Examination

Upper	93
Lower	96
Both upper	2
Both lower	5
One upper and one lower	4
Total	200

Treatments Given Before Seen by Me

None ‡	78
None	53
Massage alone	47
Brace	14
Brace and plaster	1
Plaster	3
Plexus operation	4
Total	200

Treatments Advised by Me

Brace	113
Plaster	16
Plaster, then brace	21
Massage	9
Operation	
Sever's	29
Arthrodesis	1
Plexus	2
Plexus and Sever's	4
Stretching	1
No treatments	4
Total	200

Results§	Total	Percentage	Those Treated by Me Within the First Two Months	Percentage of Total Results
Excellent (90% plus)	51	38	40	78
Very good (80 to 90%)	44	33	39	88
Good (70 to 80%)	32	24	18	56
Fair (60 to 70%)	4	3	..	..
Poor	None	..	..	..
No treatments given	64	..	.	..
Could not be traced	5	..	..	..
Total	200	Total number of patients treated by me		135

Of the eleven doubles, five were treated early. Results: excellent, 1; very good, 1; good, 3

* This large number (92) seen by me in the first month of life shows how careful both the general physician and the obstetrician are at present, of consulting the orthopedic surgeon early.

† Not always accurate as patients were not always clear about deformity in beginning.

‡ Seen by me within the first month of life; hence treatments could not begin.

§ The results of orthopedic treatment are based on a percentage schedule, giving: function, 75 per cent; contour and shape, 25 per cent.

for the shoulder to become loose. The child made a perfect recovery, with the exception of limitation to supination (fig. 5).

Comment.—The adhesions in this case were evidently due to the injury of the capsule at birth; the abducted position should not have been maintained for so long a time. This case is reported as a warning to guard against adhesions when there is evidence of injury to the capsule. It also shows the inadvisability of keeping such patients in

Fig. 6 (case 1).—Herbert A., showing how well he can hold the bow of the violin.

the abducted position for more than five or six days; massage, exercises, etc., are then given regularly, and the brace is gradually dispensed with (fig. 4).

CASE 3 (series 165).—Lawrence N. was 2½ weeks of age when referred to me by Dr. Freeman. He was the second child in the family. Birth was by breech presentation, with instrumental delivery. He had paralysis of the whole left arm. He was extremely undersized and weak. The face and skull showed signs of pressure. Right-sided torticollis was evident. A deltoid brace was applied, and in five days massage and exercises were begun. Within four months there was

very little improvement in any of the muscles, though one could feel that they were becoming firmer. As the child was extremely emaciated and undersized, one could not consider operative means, and so the orthopedic treatments were continued.

Two months later the child began to improve in general health, and then the arm began to improve. The use of the brace could not be discontinued until the child was 8 months old. At the time this article was written, when the child was 23 months of age, he was using the hand freely, even to supination. There was only a slight contraction at the shoulder and elbow. The torticollis had entirely cleared up (fig. 7).

Fig. 7 (case 3).—Lawrence N., in March, 1929, aged 1 year and 3 months. The picture on the left shows him raising the left arm. He could raise it about 10 degrees more. The picture on the right shows how he handles objects with the left hand.

Comment.—The delay in improvement was due entirely to the general debility of the child. I had many children with such conditions, and when the pediatrician was successful in putting them on the proper diet, the improvement in the paralyzed hand was rapid.

Case 4 (series 126).—Marie T. came to me at the age of 6 months with a right-sided upper type of paralysis. The child was the third in the family. The birth was not instrumental, with rapid delivery. Before coming to me, the child had had massage and exercises, but no braces had been applied.

Physical examination showed that the arm was kept in adduction and internal rotation with some contraction of the pectoralis major. She had good power in the finger.

A brace was applied, to be worn day and night. This was taken off only for massage and exercises. Within four weeks, the child could abduct the arm to right angles. Within eight weeks, the brace was dispensed with. The child made a good recovery within about three months (fig. 8).

Comment.—This patient evidently did not have a severe paralysis, but as the arm was not put in the proper position, contraction developed and she could not use the hand. As soon as the deformity was overcome and the paralyzed muscles were put at rest, recovery was rapid.

Fig. 8 (case 4).—Patient, aged 6 months, with right-sided paralysis after ten weeks' treatments, showing how far she could raise the hand.

How much easier it would have been to apply the proper brace at the very beginning.

CASE 5 (series 145).—Phoebe B was 3 weeks of age when referred to me by Dr. Levinsohn. She was the first child. Birth was by breech presentation, forceps being used. She had paralysis of both arms. She had a marked wrist drop and ulnar deviation on both sides. There was a slight contraction of both pectoral muscles.

A double deltoid brace and cock-up splints were applied, and massage and exercises were begun. Within three months, the cock-up splint could be dispensed with. Within five months, the deltoid braces were discontinued during the day. Within a year, the child used the fingers freely; she still had some contraction of the elbow. She could use the shoulder so as to put the hand to the back of the neck, but all motions of the shoulders were somewhat clumsy.

At the time of writing, at the age of 3 years, the child still used the shoulder clumsily; i. e., she brought the arm forward (adduction), bent the elbow (using

the biceps), abducted the arm and rotated it out. When she wanted to supinate the forearm, she had to keep the elbow flexed. However, the parents were doing their utmost to train the child to use the limbs better, with some success.

Comment.—This was a severe case, and while the patient is not using the hands dexterously, she is able to do all the work necessary and will probably earn her livelihood. She will surely attain better skill in using the limbs. It is doubtful in a case such as this whether the patient would have had such use of the limbs if the braces had not been used as is obtained in cases in which braces are not applied.

CASE 6 (series 191).—Leon K. was 1 day old when seen by me. There was a history of a very difficult labor, vertex occiput posterior. After the head was delivered, it took about forty-five minutes before the shoulders were delivered. Thus it can be assumed that the traction on the head was severe.

Physical examination showed complete paralysis of the upper right extremity. The right eye was closed. The head was bent to the right. There was marked tenderness at the right plexus.

Deltoid and cock-up splints were applied and treatments instituted. In spite of careful treatment, the child showed absolutely no improvement within the first three months. I became discouraged and sent the child to a neurologic surgeon for consideration of a plexus operation. He, however, thought that the case was beyond hope, and that it was futile to operate. He advised continuing the orthopedic treatments for three months longer.

At the end of that period, there was quite an improvement in the deltoid and biceps muscles. The use of the deltoid brace was discontinued when the child was 10 months of age. The cock-up splint was still used. At the time of writing, when the child was 1 year old, he could use the shoulder and forearm well. The wrist had a slight tendency toward flexion. He had some power of flexion in the fingers, though not enough to grasp things.

Comment.—This patient showed no improvement for the first three months; yet with persistent treatment preventing the stretching of the paralyzed muscles, improvement was obtained. What would have happened to the child had he been left without braces is easy to surmise.

CASE 6 (series 20).—Charles D., aged 7 years, came under my observation on May 8, 1920. There was paralysis of the right side (upper type) with marked contraction of the pectoralis major and teres major muscles. He could not abduct the shoulder voluntarily more than to an angle of 25 degrees.

He was operated on on May 19 at Fordham Hospital by Dr. Taylor and myself. Sever's operation was done (tenotomy of the pectoralis major and subscapularis). The plexus was then exposed, and only two small neuromas over the fifth and sixth cervical roots were found; the fascia was freed, but no nerve suture was performed. There was, therefore, distinct evidence of nerve injury.

I watched him for about one year, and he had good use of the upper extremity (figs. 9 and 10*A*). I then lost track of him. He returned in January, 1929. During this time, he graduated from elementary school and attended high school; at the time of writing he was in the seventh term. He was able to do the general work like other boys, but could neither write with the right hand nor use the elbow freely.

Fig. 9 (case 6).—Charles Angela D., on Dec. 2, 1922, showing good power of abduction, rotation outward and supination after the first operation and treatments.

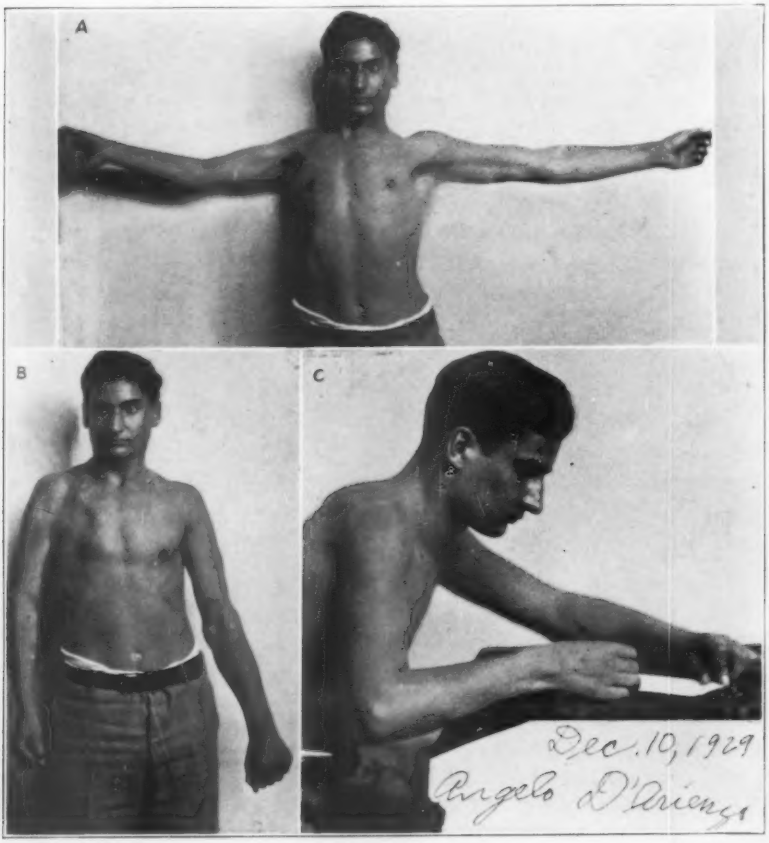

Fig. 10 (case 6).—Charles Angela D., on Dec. 10, 1929. *A* shows that the improvement obtained at the first operation was retained. *B* shows the ability to extend the elbow and bring the arm in pronation. *C* shows the position of the hand for writing and a specimen of handwriting.

Physical examination showed a healthy young boy. He could abduct and rotate the right shoulder to about 80 degrees. He extended the elbow to an angle of 155 degrees. The forearm was in complete supination, and the patient could not pronate at all. (This is contrary to the usual deformity.) In view of the contraction of the biceps muscle, I concluded that that was responsible for the deformity. He used his left hand for writing, eating and combing himself.

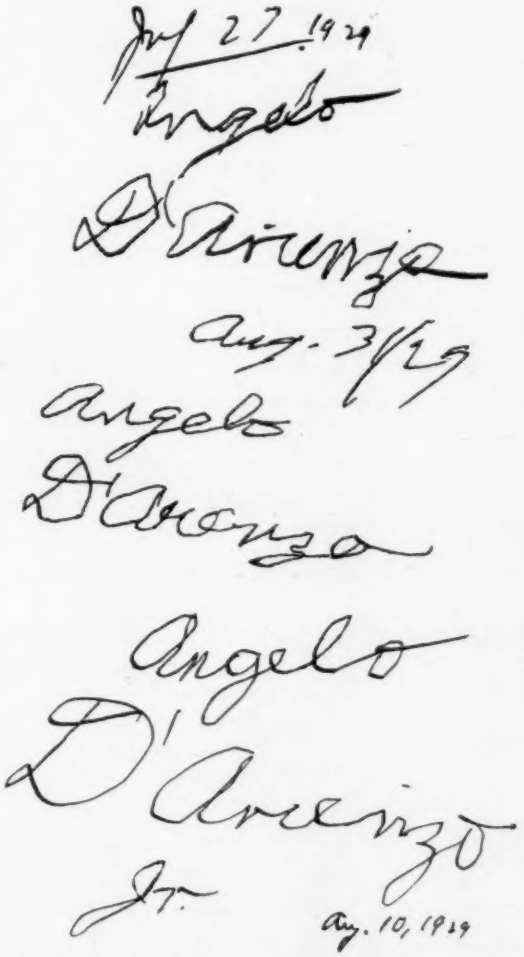

Fig. 11.—The handwriting of Charles D. at different times after the second operation.

I operated on him in July, 1929, when I cut the fibrous bands from the biceps muscle to the ulna; I then transplanted the outer head of the biceps muscle to the posterior aspect of the radius; the forearm was put in pronation and extension, as I hoped at first to correct the flexion and perhaps gain some power to pronate.

The plaster was bivalved within two weeks; massage and exercises were started. Within two weeks, the patient attempted to sign his name (fig. 10*C*).

Within four weeks, the writing improved. When he returned to school, he obtained permission to use his right hand for writing, although it might take him longer. He found, however, that within the first week he could keep up with the class (fig. 11 shows his handwriting). At the time of writing, he could use the right hand for everything. The elbow could be extended fully.

Comment.—This case demonstrated that (1) there was a nerve injury; (2) the lack of motion at the first instance was due entirely to the contraction of the pectoralis major and subscapularis; (3) the supination and flexion of the elbow were due to the contraction of the biceps muscle. The rapid improvement after the operations proves that the deformities were responsible for the inability to use the limbs.

Had the child been treated properly with orthopedic measures from the beginning, he would have made a perfect recovery, as the nerve regeneration was good, and the muscles were not markedly paralyzed.

CONCLUSIONS

1. If these patients are treated early and properly, one may expect good recovery within three or four months in mild cases.

2. The more severe cases require about six or seven months for complete recovery.

3. The shoulder should be put up in a splint of brace immediately to prevent stretching of the paralyzed muscles and contracture of the unopposed muscles.

4. When there is a weakness of the wrist, a cock-up splint should be used.

5. The armamentarium of the obstetric service of the hospital should include the braces or wire splints necessary for immediate attention in these cases.

6. The support may have to be kept on for a very long time, eight or nine months, as deformities may occur. Of course, massage and exercises are begun early.

7. Massage and exercises alone are not sufficient.

8. Even in the whole or the lower type of paralysis, one may try conservative treatments for a while and then resort to a plexus operation. The result is not so discouraging as some textbooks would lead one to believe.

9. The joints must be watched for stiffness.

349 East 149th Street.

THE PRACTICE OF INOCULATION RECOMMENDED IN A SERMON BY THE REVEREND WILLIAM DODD, 1767

JOSEPH H. MARCUS, M.D.
Pediatrist to Atlantic City Hospital
ATLANTIC CITY, N. J.

In the year 1721, vaccination against smallpox was introduced into England by Lady Mary Wortley Montague, wife of the British ambassador to Turkey, whose 3 year old son was successfully inoculated in Constantinople, where the procedure had been in use for nearly a century. When it was first introduced into England, some of the clergy were among the formidable opposers and publicly preached against the practice as highly sinful. The Reverend Mr. Massey at St. Andrews, Holborn, on July 8, 1722, using as his text, Job ii, 7, preached against inoculation as derived from the devil, Satan being the first inoculator when he smote his victim with boils. However, it was after Jenner's immortal discovery, when it became obvious that smallpox was deprived of its accompanying terrors, that parliament ordered "that every infant shall be vaccinated within three months after its birth, unless the state of its health should render the operation objectionable." About this time, the Reverend Increase Mather published a document in which were expounded "various reasons for proving that inoculating or transferring smallpox is a lawful practice." Among the arguments that he adduced are the direct benefits derived from it, and he referred to the fact "that we have an army of Africans among ourselves, who have themselves been under it and given us all the assurance which a rational mind can desire; that it has been used with success in Africa." (Vaccination was used in Africa before its adoption in Great Britain or America.)

One of the ardent disciples of inoculation was The Reverend William Dodd, who delivered a sermon on April 9, 1767, twenty-nine years before Jenner performed his first successful vaccination.

The printing and distribution of this pamphlet were authorized by the "Governors of the Hospitals for the Smallpox Inoculation." The Reverend Dodd used as his text, Proverbs xiv, 28. (In the multitude of people is the King's honour, but in the want of people is the destruction of the Prince.)

It is strange to think how much Men's Ideas of true Honour have been vitiated, and with what a blind Enthusiasm those names have been venerated from the earliest Antiquity, are venerated in all Times, whose chief Praise is the Lust of Conquest, and the savage Destruction of their Species. Real Honour of a King consists not in spreading around Ruin and Devastation, under the pretense of

THE

PRACTICE of INOCULATION
RECOMMENDED,

IN A

SERMON,

PREACHED

At ST. JAMES'S, WESTMINSTER,

April the 9th, 1767,

ON THE

ANNIVERSARY MEETING

OF THE

GOVERNORS

OF THE

SMALL-POX HOSPITALS.

By WILLIAM DODD, LL. D.

Prebendary of BRECON, and Chaplain in Ordinary to his MAJESTY.

LONDON:

Printed by W. FADEN, *in Fleet-Street*; and sold for the Benefit of the Charity.

Conquest and Glory; but in multiplying, and in Blessing; in augmenting the Number, and the Happiness of his People.

He urged the institution of any measure that would benefit mankind:

by encouraging those Virtues, which are most conducive to Health and Life; and above all, by inculcating the Exertion of those Charitable Efforts, which have immediately in View the salvation of the Body as well as of the Soul.

In the seventeenth century, the ravages of smallpox caused innumerable deaths. Dodd stressed its vast importance in the following words:

> That Population is diminished amongst us, and that due Endeavors are not applied to encourage and increase it. If this is the Case,—which for my own Part, I cannot but greatly doubt,—There is certainly the more Need to support with redoubled Vigour all those Efforts, which tend to Population, by the *Preservation of Life.*

Realizing the economic factors, as well, in the vast number of mortalities, he said:

> Let any man then consider what an abundant, what an amazing Saving to the Community these lives would have been, had it been possible by any Heaven-taught Art, by any Discovery from the Goodness of God to Man, to have baffled the Force of this dire Disease, to have discovered where the strength of this mighty *Sampson,* this invincible Destroyer lay! And in Case of such a Discovery, is it possible to suppose, that any Human Creature should reject the Celestial Gift, should choose to suffer all the Depredations of the Disease, to run all the fearful Chances of its unrelenting Fury, rather than *wash in this Jordan, and be clean?*

Credit is also relegated to the Divinity for the discovery and use of vaccine:

> Human Art, enlightened and assisted by the Divinity, hath found out a Method, next to infallible, of preventing all the Horrors, and all the fatal Consequences of this pernicious Disease.

On the relationship of the infliction of disease as a punishment for evil, he conjectured:

> We can see many Reasons for the infliction of Diseases,—those Correctors of Evil, those Admonitors of Good. Besides, Diseases are often not the Inheritance of our Nature, but the Punishment of our Sins; in this case vindicating the Deity, and arraigning our own Indiscretions.

He urged the Governors of the Hospitals to institute measures for properly regulated procedures for inoculation, so as "to prevent the Evils which arise from the partial, promiscuous and irregular Practice of this Art." He urged the importance of isolation, saying the danger of the spread of contagion lies in allowing "those who have the Distemper upon them and are suffered to range at large in our Streets and Villages, to communicate the pestilential Disorder to others." He further admonished that all the patients should be secreted within the hospital walls until all danger of infection was passed.

In appealing to parental solicitude, he said:

> Let the tender, the affectionate Parents, while they look with Eyes melting in Tears of Joy, on their beloved Offspring around them, preserved by the Practice of this heaven-born Art from the foul Ravages of a Disease generally fatal to Beauty, or to Health, if not to Life; . . . The Father, the Husband, sink

beneath its cruel rage! Wretched Widow! who shall assuage thy Sorrow! Miserable Orphans, who now shall be your Comforter and Support! How happy for you all, if in early Youth that life-preserving Art, we are recommending, had been applied.

After appealing to his audience as patriots and men, he advanced his dissertation from an angle of Christianity:

A Love for Souls, and a Desire of their Salvation. For who can be ignorant into what fearful Peril of their Eternal Loss those Souls are plunged, which, seized in a natural Way, are hurried,—affrighted and aghast!—from this Life to the next, "with all their Imperfections on their Heads;" unrepentant, unprepared; their temporal and their eternal state alike unprovided for!

In a preamble arousing their charitable sympathies, he concluded by saying:

You cannot surely at all justify yourselves, or find any Comfort within, if you employ your Wealth without any Reserve upon Self-Gratifications, and with-hold it, with a hard and parsimonious hand, from the tender offices of Humanity and brotherly Love. . . . Think what a Satisfaction you will enjoy here-after, when the mighty Master, the aweful Judge and Arbiter of your Fate, shall stamp that Improvement with his Applause, and admit you to the Transports of his eternal Kingdom with the enrapturing Words, WELL DONE, GOOD AND FAITHFUL SERVANT; ENTER THOU INTO THE JOY OF THY LORD!

101 South Newton Avenue.

Pediatric Biographies

JÓZSEF CSAPÓ
1734-1799

JOHN RUHRÄH, M.D.
BALTIMORE

In Hungary, as elsewhere, the diseases of children were treated by the physicians after the manner prescribed in the textbooks in use in other countries. Infant mortality was high, as it is in parts of Hungary today; but the women were prolific, and neither the loss of infant life nor the enormous losses entailed in more or less constant warfare prevented the progress of the race. Rosenstein's book was translated into Hungarian by Samuel Domby and published in 1794, but long before this a Hungarian physician had written a book on the diseases of children and infant care which was published in the native tongue, although it appeared years later in a Latin translation.

József Csapó [1] was born July 18, 1734, at Györ. His father was a lawyer in the service of Fürst Eugen of Savoy, and his mother was Maria Ott. He received a good education, as befitted his station in life, first in the public schools of his native town and then in the universities in Germany and Switzerland. He also traveled in France. On Aug. 7, 1759, he received his doctor's degree in Basle, defending a dissertation in Latin, "De febre Hungarica." He then settled in Debreczen, where he became chief physician, and there he practiced for the remainder of his life. He died in 1799.

He wrote a number of books, only two of which were on diseases of children. There is a manuscript in the Magyar Nemzeti Museum, in Budapest, which contains, in addition to his valetudinarum infantile, an account of a "monstrum bicorporum humanorum," which was furnished him together with a description by Dr. Christian Weinmann, a surgeon.

His first book was published in 1771 at Nagy-Károly and is entitled, "Kis gyermekek isputálija, melyben Különbféle nevezetes nyavalyái és külsö hibái a kis gyermeknek és ezek eránt lehetö orvoslásnak módjai hüségesen megirattak." It is an octavo of 122 pages. The title may be translated as, "A Treatise on the Diseases of Little Children in

1. Csapó József s gyermekyogyászati munkai. Irta: Györy Tibor dr. Budapest, 1903. This appeared in the Orvosi Hetilap, and Dr. Janos Geldrich, of Budapest, read it to me.

Which the Well Known Diseases and the Manifest Defects of Infants are Considered and the Treatment Stated." This book was translated into Latin with some additions about twenty-three years later and appeared in Pest in 1794 in an octavo form of 188 pages. It was published by Francisci Aug. Patzko. The Latin edition bore the title, "Valetudinarum infantile Hungaricum novum, sistens morbos infantium centenos, horumque tutos curandi modos subjunctis instructionibus cautelisque utillissimis centenis."

KIS GYERMEKEK

ISPUTALJA,

Mellyben

Kûlömbféle Nevezetefsebb Nyavalyái, és kûlsô Hibái a' kis Gyermekeknek, 's ezek ellen lehetô orvoslásnak módgyai bôségefen meg-irattak.

CSAPO JOSEF

Medicinæ Doctor, és Nemes Szabad Királyi DEBRECZEN Városának Physikusa által.

N. KÁROLYBAN.

Sz. N. PAP ISTVÁN Typographiá által 1771 Eſztendôben.

This edition includes five sections. The first one contains separate chapters on the diseases of children. Then follows an article on the treatment of the new-born infant, a section on breast feeding, one on weaning and lastly useful rules on the upbringing of children. These rules are of great interest, and show that Csapó was a shrewd observer and full of common sense. A few excerpts will illustrate the nature of his advice.

1. The milk of the mother is better for the child than that of a wet nurse, for with the milk the child also absorbs the mother's love. It is also decreed by nature that it is better to be nourished in milk made from the same blood as formed the child in utero.

2. The mother should not nurse from one side only lest the child be crooked as the back may be deformed by one sided nursing.

3. The child should not be rocked too much or too violently lest the brain of the child be shocked and hicket and vomiting result.

4. If the child is allowed to stand on its feet too soon it will have crooked legs.

5. It is harmful to give wine or spirits to the child as it will interfere with the growth and affect the brain so that the child will be stupid.

6. Sleep producing drugs should not be given as the body will be injured and the mind weakened.

7. When the child sweats it is dangerous to take it out of the crib and expose it suddenly to cold as it may catch cold or cause colic, diarrhea or even death.

8. When children have either coryza or diarrhea they should wear stockings and the abdomen should be kept warm both day and night.

9. After birth the child should be washed, not in milk, but in clean luke warm water. Eventually one third pure wine may be added.

10. Children should not be allowed to sit too long on the chamber pot lest the rectum come out.

11. The body should not be annointed with oil for it will hinder the necessary perspiration and so many diseases may be caused.

12. The child should not be bound too closely lest it make it restless.

13. Do not carry the child by the arm lest the tendons be stretched and the arms dislocated.

14. When the mother is frightened she should not nurse the child at the breast, nor when she is ill.

15. A very angry woman should not nurse the child or if she does the first milk of the breast should be drawn off before.

16. When a woman is sad her milk will be spoiled and the child will fade away.

17. The woman should not eat too much lest the nursling take too much salty material with the milk and so have skin eruptions.

18. One should not permit the wet nurse, especially if she is old, to chew the food for the child, as from such food little children often are killed.

19. The child should be trained early to sleep more in the night than the day.

20. The day on which the wet nurse takes medicine she should nurse the child before and sufficient to last the day.

21. When the wet nurse menstruates another woman should nurse the child.

27. One year is long enough to nurse the child; after that it should be weaned.

34. Disease may be caused by unsuitable food; such things should be withheld.

38. Small children should not be purged with aloes.

41. As a child is brought up so will it be when grown. It is, therefore, not good to frighten little children but rather to encourage them.

Correspondence

ANEMIA OF THE NEW-BORN

To the Editor:— Concerning the interesting case report, Anemia of the New-Born (Am. J. Dis. Child. **39**:807 [April] 1930), may I take the liberty of calling Dr. Gelston's and Dr. Sappington's attention to the fact that their bibliography is incomplete and that cases of this condition have been reported in excess of the number they have mentioned. I spoke on this subject at the Fifth Pan-American Child Congress, in Havana in December, 1927, and my contribution was published in the *Archivos americanos de medicina* in April, 1928 (vol. 4, p. 39), and is indexed in the Quarterly Cumulative Index for that year. The title was "Anaemia primitiva en los recien nacidos."

While Gelston and Sappington report seven cases as being reported up to 1929, up to September, 1927, ten cases were reported in medical literature, including two which I mention in "Diseases of the Newborn" (Philadelphia, J. B. Lippincott Company, 1926, p. 59), and an additional one which I found in one of premature twins and which was studied in the particular paper mentioned in the foregoing paragraph. Since that time I have seen two other patients in private practice suffering from the same condition.

May I also point out that the second case of this condition, and not the third, was reported by Donnally in 1924, and that the first report by Ecklin was rather a casual record, while Donnally's study was thorough in every detail, including a complete history and examination of both parents and the usual blood count studies, fragility tests, Wassermann reaction, reticular cell counts, comparative measurement of erythrocytes and other data which proved that the disease was actually primary anemia.

I have endeavored to establish similar facts on the five patients whom I have studied, and I am convinced that so-called primary anemia is identical in every way with the "blood depot exhaustion" anemia seen in premature infants, except that it is usually greater in degree and therefore more violent in its manifestations than the anemia of prematurity.

This fully corroborates Donnally's conclusion that such infants are normal at birth so far as the hemoglobin and erythrocyte count are concerned.

That this anemia is manifested in varying degrees of severity is shown by Bonar's patient, who recovered spontaneously after a year, while Donnally's patient and one of mine, as well as the infant treated by Gelston and Sappington, required repeated transfusions to stimulate the blood-forming mechanism to normal functioning.

At the meeting of the Section on Pediatrics of the Southern Medical Association last November, Josephs reported the successful treatment of a number of young infants, some of whom had primary anemia, with salts of copper and iron and with emulsion of liver.

The condition of so-called primary anemia occurring not at birth, but within one or more weeks after birth, is therefore not uncommon, and will be still better known when it is looked for with more constant regularity. It is perhaps not wise to call it primary anemia, since it is not present at birth, but comes on with varying intensity when the apparently insufficient blood depot supplied by the mother has been exhausted. Whether or not this rapid exhaustion depends on an essential failure of the blood-making mechanism so far has not been established.

John Foote, M.D., Washington, D. C.

To the Editor:—May we express to Dr. Foote our regret at the oversight of his valuable work in anemia of the new-born? We appreciate very much his bringing this to the attention of the medical public, since complete bibliographies are essential in articles of this nature.

Incidentally, there have been two publications in 1930 on primary anemia of the new-born: Greenthal, Roy M.: Am. J. M. Sc. **179**:68 (Jan.) 1930. Happ, W. M.: Arch. Pediat. **47**:171 (March) 1930.

C. F. GELSTON, M.D., San Francisco.

"DIGITALIS STUDIES ON CHILDREN WITH HEART DISEASE"

To the Editor:—I was much interested in reading Dr. Sidney P. Schwartz and Dr. John B. Schwedel's article entitled "Digitalis Studies on Children with Heart Disease," which appeared on pages 298 to 315 of the February number of the AMERICAN JOURNAL OF DISEASES OF CHILDREN. The conclusion that "nausea and vomiting cannot be used as criteria in estimating the optimal therapeutic dose of digitalis for children with chronic rheumatic valvular heart disease and signs of heart failure" reminds me of the negro convict's lawyer who told his client that he could not be arrested for the crime with which he was charged. The negro replied, "That may be so, boss, but here I is." The studies which A. W. Jacobsen and I made four years ago (AM. J. DIS. CHILD. **32**:373 [Sept.] 1926) demonstrated that nausea and vomiting not only could be but were used successfully as criteria in estimating the optimal therapeutic dose of digitalis for children.

WILBURT C. DAVISON, M.D., Durham, N. C.

To the Editor:—I am well acquainted with Dr. Davison's excellent paper mentioned in his letter. I discussed his work and that of his associates, Jacobsen and Leonard, in a paper which I recently read before the Journal Club of Montefiore Hospital. I am withholding publication of this paper in order to repeat my experiments (similar to those of Davison) on the children studied.

SIDNEY P. SCHWARTZ, M.D., New York.

CORRECTION

In the article entitled "The Comparative Value of Toxoid and of Other Agents in the Immunization of the Preschool Child Against Diphtheria," by A. B. Schwartz, M.D., and F. R. Janney, M.D., Milwaukee (AM. J. DIS CHILD. **39**:504 [March] 1930), reference was made on page 507 to Schick tests "done with material prepared by the New York State Board of Health Laboratories." This should have read "the Laboratories of the New York Department of Health."

News and Comment

UNIVERSITY NEWS

The pediatric department of the University of Colorado Medical School offers a fellowship with remuneration of $100 a month without maintenance, the duties to consist of service in the pediatric ward of the Colorado General Hospital and in the outpatient department, with opportunity for research.

Harvard Medical School is offering postgraduate work in pediatrics as follows: Course *A*, one month (June): fee $125.00 all day; $80.00 mornings only; $60.00 afternoons only; $80.00 with lectures and pathologic conferences. Course *B*, from October to May inclusive, number limited: fee $600.00.* Registration fee for each course is $5.00.

Dr. Maynard Ladd, Harvard University Medical School Courses for Graduates, Boston, is in charge of this work.

* In the May issue, the fee for Course B was given as $6.00 instead of $600.00.

GENERAL

Five Years of Municipal Infant Welfare in Amsterdam.—The medical statistical department of the Municipal Health Service of Amsterdam (Holland) has issued an important statistical study on the work done by the Municipal Infant Welfare division during the first five years of its existence. The booklet contains a description of the splendid organization of the division. Further, it gives extensive statistics on the babies that came to the consultation bureaus during these five years.

Postvaccinal Encephalitis in Holland.—Between July and October, 1929, 47 cases of postvaccinal encephalitis occurred in a total number of 79,154 children vaccinated in Holland (i. e., 1 case in 1,684). In 8,652 children, however, who were vaccinated before the age of 1 year not one case of encephalitis occurred. Since 1924, the frequency of postvaccinal encephalitis has increased decidedly, except in children under the age of 1 year. With increase in age the possibility of encephalitis after vaccination increases, as may be deduced from the following figures concerning vaccinations performed between July and October, 1929.

One case of encephalitis occurred in each of the following numbers of vaccinations:

Age	Vaccinations
0-1	....
1-2	3487
2-3	1759
3-4	1423
4-5	1560
5-6	1468
6-11	815

Therefore, in Holland if vaccination is performed for the first time after the age of 6, the chance of getting encephalitis is four times as large as if the vaccination is performed before the age of 2 years. Under the age of 1 year the chance is still less.

Memorial to the Late Dr. John Thomson.—On Dec. 14, 1929, a marble panel with an inscription and a bronze portrait-medallion was unveiled in the

Children's Hospital, Edinburgh. The ceremony was performed by Sir Thomas Barlow. The remarks made by the various speakers (Sir Thomas Barlow, Prof. G. F. Still, Dr. A. Logan Turner, Sir Robert Hutchison and the Very Rev. J. Harry Miller, D.D.) are printed in the *Edinburgh Medical Journal* (February, 1930) and show great reverence for Dr. Thomson and appreciation of his life, which has been spent in the Children's Hospital. Mention is made of his early translation of Henoch's treatise on children's diseases, his clinical teaching at the university, his early description of pyloric stenosis, his membership in the small society known as the "C.C.C." or Clinical Club for the Study of Children's Diseases. His little book, "Opening Doors," dealing with the types of mental deficiency in children, has become of great interest to the mothers of such children. His university gave him the degree of Doctor of Laws, and the Royal College of Physicians of London gave him the rare distinction of a fellowship. Just before his death he finished a revision of his well known book on children's diseases. A photograph of the memorial panel is reproduced in the *Edinburgh Medical Journal*.

Resident Pediatrician Needed for Children's Memorial Hospital, Montreal.—Applications are invited for the position of resident in the department of pediatrics for one year from Sept. 1, 1930; the salary is $300, with board and laundry. The pediatric service offers a wide variety of clinical material and is affiliated with McGill University for teaching purposes. The total capacity of the hospital from Sept. 1, 1930, will be 200 beds. The routine medical care of all surgical cases is entrusted to the pediatric department. Daily rounds are made by members of the senior staff. General rounds, under the direction of the professor of pediatrics, are conducted once a week. Applicants must forward their photographs and credentials before July 1 to Dr. Henry P. Wright, secretary, Pediatric Medical Board.

Bequests and Donations.—The Children's Orthopedic Hospital, Seattle, received $3,000 by the will of the late Dr. Roy C. Baumgarten.

The Home for Destitute Crippled Children, Chicago, was given $5,000 by the will of the late Miss Grace Dixon.

DEATHS

On April 24, 1930, Prof. Carl Leiner of Vienna died suddenly after a brief illness, at the age of 59. He studied in Vienna and Prague and obtained his dermatologic training as a pupil of Kapossi and his pediatric training as a pupil of Knoepfelmacher. At the time of his death, he was associate professor of pediatrics and attending physician in the Mautner Markhof'sch Children's Hospital of Vienna. His principal field of research was pediatric dermatology. He had a delightful personality, was an excellent teacher and was beloved by all his students. It was as a matter of course that every American physician studying in Vienna took his courses given on Saturdays, in his hospital.

He described erythrodermia desquamativa in early infancy, a disease which bears his name. He introduced the intracutaneous method of vaccination for smallpox, which marked decided progress and is widely used in different countries. His experimental studies, conducted with Wiesner, on poliomyelitis are also well known. Leiner published many papers dealing with almost every dermatologic disease in childhood. His article, "Skin Diseases in Infancy," appeared recently in the Handbook of Dermatology of Jadassohn. His death is a real loss to pediatrics.

Abstracts from Current Literature

Anatomy and Physiology

ANATOMIC GROWTH OF CHILDREN. B. T. BALDWIN, L. M. BUSBY and H. V. GARSIDE, University of Iowa, Studies in Child Welfare **4**:1 (Oct. 1) 1928.

These data were taken from 1,300 roentgenograms of the epiphyses of the hand and the lower forearm, the sesamoid bones of the hand and the bones of the wrist. Physical measurements were taken on or near the date that the roentgenograms were made. The girls were in advance of the boys in time of the first observation and infusion of the epiphyses of the hand and the lower forearm. The metacarpophalangeal sesamoid bones of the thumb ossified two years later in boys than in girls. The general skeletal size of the child was found to be a factor in judging the anatomic maturity from the area of the ossification of the carpal bones. The boys had not reached a maximum mean anatomic index by 17 years; the girls reached a maximum mean by 15 years.

SANFORD, Chicago.

CONGENITAL SCOLIOSIS AND DOLICHOCEPHALY AS CORRELATED DEVELOPMENTAL DEFECTS. DAVID M. GREIG, Edinburgh M. J. **36**:709 (Dec.) 1929.

Mr. Greig, conservator of the Royal College of Surgeons' Museum, Edinburgh, describes and discusses in forty pages of this issue a specimen showing congenital scoliosis, a cleft spine, a long head, deformities in and around the foramen magnum, a primitive pelvis, costal suppression and fusion, and deformity of the sternum. These abnormalities belonged to an idiotic girl who died at 8 years of age.

Greig believes that these numerous deformities illustrate a series of interdependent malformations originating in an embryonic disturbance in the vertebral growth which dates from the first three or later weeks of fetal life. Experiments in embryology have produced perversions of this sort by an influencing factor affecting the environment, such as the temperature, chemical agents, roentgen rays and radium. The scoliotic deformity occurred earlier than the spina bifida and may have been the cause of the latter.

Spina bifida is commonly associated with hydrocephalus, but in Greig's case the head is not that usual shape, though he believes that nevertheless it is definitely hydrocephalic. He does not admit that the abnormally long, narrow type of skull is due to premature ankylosis of the interparietal suture, as was once thought. He believes that the brain molds the shape of the growing skull, for as long as the brain is growing, the sutures retain their function. In this specimen all the sutures, especially the sagittal and frontal, are present and functioning. The explanation of the elongation of the brain and secondarily of the skull may be found in the abnormal fixation of the spinal cord with resultant traction on the cerebral peduncles, for this promotes an extension of the cerebrum posterior to the base of the occipital bone.

NEFF, Kansas City, Mo.

THE NUMBER OF BLOOD PLATELETS IN NORMAL INFANTS. STEN ECKERSTRÖM, Nourrisson **18**:26 (Jan.) 1930.

In this investigation the technic of Kristenson was used. The blood of infants varying in age from 8 hours to 6 days was examined. Ninety-one counts were made on forty-six infants. The average count on infants less than 24 hours old was 180,000. Each day showed a gradual increase until at the age of 6 days the average reached 250,000. When counts were made on successive days on

the same baby a similar increase was found. Other observations were made on infants ranging in age from 1 week to 1 year. These counts increased from approximately 300,000 to 400,000.

McClelland, Cleveland.

Pathology, Bacteriology and Biochemistry

Hypersensitiveness to Arsphenamine in Guinea-Pigs: I. Experiments in Prevention and in Desensitization. Marion B. Sulzberger, Arch. Dermat. & Syph. **20**:669 (Nov.) 1929.

The skin of guinea-pigs was sensitized to neoarsphenamine by intradermal injections of the drug. The hypersensitivity showed itself by a flaring up of the area of injection from six to fifteen days later, and by a reaction of hypersensitivity to a second intradermal injection given thirty-one days after the first. Neoarsphenamine given intracardially within twenty-four hours after the potentially sensitizing injection prevented the appearance of the hypersensitiveness, although it did not do so when given the fifteenth day. Administration of gold sodium thiosulphate intracardially on the fifteenth day did not effect desensitization.

Shirley, Iowa City, Iowa.

Blood Formation of the Albino Rat on a Standard Dietary Régime. Barnett Sure, M. C. Kik and D. J. Walker, J. Nutrition **1**:299 (March) 1929.

Albino rats were fed on a diet consisting of whole wheat 27 per cent, rolled oats 26 per cent, yellow corn 25 per cent, oil meal 15 per cent, commercial casein 5 per cent, cod liver oil 1 per cent, sodium chloride 0.5 per cent, sodium carbonate 0.5 per cent and a liberal supply of fresh whole milk daily. Hemoglobin determinations and erythrocyte counts were made from the day of birth until the three hundred and fortieth day. Age plays a determining rôle in the concentration of hemoglobin and erythrocytes in the blood of the albino rat during the period of growth. Sex plays a relatively insignificant rôle. The total leukocytes varied so widely in individuals at different stages of growth that the influence of age and sex could not be determined. On the diet described, pregnancy produced anemia which was marked on the day of delivery, but which disappeared with the advance of lactation. A marked drop in serum proteins occurred late in pregnancy. The concentration of hemoglobin and red corpuscles in the lactating rat is greatest near the weaning period of the young when the nurslings begin to partake of the maternal diet.

Kugelmass, New York.

Vitamin Requirements of Nursing Young: VII. The Production of Uncomplicated Vitamin B Deficiency in the Nursing Young of the Albino Rat. Barnett Sure and Margaret E. Smith, J. Nutrition **1**:537 (July) 1929.

A biologic technic is described. A ration that furnishes as much as 10 per cent autoclaved yeast must contain sufficient undestroyed vitamin B to keep the nurslings that partake of the maternal diet at maintenance for a considerable length of time. The technic is varied to produce the various desired phases of the avitaminosis in nursing young in order to study the biochemical changes in the blood and tissues. The pathologic lesions of uncomplicated avitaminosis are: severe hemorrhages in the vertebral column; hypertrophy of the heart, particularly of the right auricle; liver atrophy, and capillary congestion. All the animals showed either progressive hypoglycemia or an accentuated form in the premortal state. Constipation was present. The liver showed a marked reduction in glycogen content. Anhydremia, associated with disturbance in hematopoietic function, has also been found in polyneuritic nursing young.

Kugelmass, New York.

DEHYDRATION. JAMES L. GAMBLE, New England J. Med. **201**:909 (Nov. 7) 1929.

The author shows by diagrams: (1) the relationships of body fluid compartments, (2) the amounts of acid and base ions in respective body fluids and digestive secretions and (3) the cause of alkalosis by loss of gastric secretions and acidosis by loss of pancreatic secretion. Volume loss in dehydration is dependent on a primary event, substance loss, which is mainly in the form of sodium and chlorine ions. Therefore, to replace volume it is necessary to replace the substances mentioned. The substance lost in the dehydration mechanism occurs with gastrointestinal secretions lost following vomiting and diarrhea. This hypothesis is proved experimentally. When these secretions are lost there is a parallel loss of total substances and of water from the blood. In severe dehydration, plasma volume may be reduced by one-third. This is possible only at the expense of the reservoir of volume contained in the interstitial compartment of the tissues which contains the substances sodium and chlorine. Blood plasma, too, contains like substances and shares in the loss of volume present in dehydration rather than tissues not containing the sodium and chlorine ions. Unless the relative amounts of these substances lost agree with the ratio of concentrations in the blood plasma there must result a compensating alteration of plasma bircarbonate which in turn produces a change in reaction. Clinically, this is manifested by acidosis and alkalosis in cases with diarrhea and vomiting, due to excessive loss of the sodium and chlorine ions in varying amounts. In vomiting, chlorine is lost, with an increase of plasma bicarbonate and a resulting alkalosis. In diarrhea the sodium ion is lost, and acidosis results.

To combat the two conditions mentioned it is necessary to replace the substances which control tissue volume combined with sufficient water to constitute the volume. This is accomplished by giving solution of sodium chloride subcutaneously and about from 15 to 20 cc. of a 10 per cent solution of dextrose intravenously to assist in rebuilding the blood plasma by its hypertonicity and the resulting decrease in the absorption time of the salt solution. The dextrose solution also assists in renal function adjustment, so necessary in the regulation of the respective amounts of sodium and chlorine ions to be retained. The author discourages the use of the intravenous injection of bicarbonate in cases of acidosis.

THE SIGNIFICANCE OF KETOGENESIS. A. B. MACALLUM, Canad. M. A. J. **22**:3 (Jan.) 1930.

The author gives a detailed explanation of his theory of ketogenesis. Of all the beta-hydroxy and beta-oxy acids formed in the metabolism of fat from its fatty acids in the beta-oxidation process in the human body, only beta-hydroxybutyric and beta-oxybutyric acids are readily soluble in water and are therefore diffusible from the cells engaged in this metabolism.

The oxidation systems in the fat metabolizing cells are not unlimited in the oxygen they command at any one time. Consequently, oxidation in them is controlled by the supply which is constantly replenished from that in the blood, but to a degree not beyond the maximum that these cells are capable of receiving and utilizing from moment to moment.

If dextrose is present in sufficient amount or in a condition capable of being oxidized, the amount of oxygen available for oxidation of fats is reduced to the point that only moderate quantities of beta-hydroxybutyric and beta-oxybutyric acids are formed. These are oxidized before they can diffuse out of the cells.

If the sugar is not present or, as in diabetes, if it is in a state incapable of being oxidized, the oxygen available is utilized in oxidation of the fats. The result is that a large amount of beta-hydroxybutyric and beta-oxybutyric acids are formed, and the diffusion pressure becomes so great that in more or less considerable quantities they pass into the blood.

Dextrose and its congeners are, therefore, "antiketogenic" only in the sense that their oxidation in the cells of the normal subject lessens the amount of fat

oxidized in them, and accordingly the amount of ketones formed is reduced to what the cells can burn before any but negligible traces can diffuse out of them.

MOORE, Omaha.

GAS TENSIONS AT THE SKIN SURFACE OF MAN. J. A. CAMPBELL, J. Physiol. (Proc. Physiol. Soc.) **67**:viii (Feb.) 1929.

When the hand and the lower forearm were enclosed in a glass cylinder in such a way that gaseous equilibrium could be attained between the gas of the cylinder and the skin, carbon dioxide equilibrium was reached at about 40 mm. carbon dioxide tension. At oxygen tensions of less than 50 mm., oxygen diffused neither into the hand nor out of it. At tensions above 50 mm., oxygen slowly diffused in. The conclusion is that the skin is impermeable outward to oxygen.

KUGELMASS, New York.

THE ELIMINATION OF KETONE BODIES IN THE CHILD. AUGUSTE CHAMEIX, Thèse de Lyon, 1929.

Following a discussion of the conceptions of acidosis up to the present time, the author reports his results in a study of thirty-eight children. The methods of Fleury and Guillaumin gave comparable results for acetone, and the method of Hubbard-Guillaumin was used in determining beta-oxybutyric acid. Beta-oxybutyric acid is usually eliminated in greater quantities than other acetone bodies in diseases accompanied with acetonuria. In febrile conditions, particularly in pneumonia, the elimination of ketone bodies is accompanied by an elevation of the coefficient of Maillard Derrien, i. e., the relation of ammonia nitrogen to total nitrogen. In nonfebrile conditions, except diabetes, this does not occur. The normal child eliminates 3 mg. of acetone per liter of urine and 21 mg. of beta-oxybutyric acid.

LESLIE, Evanston, Ill.

THE INFLUENCE OF DIET ON BLOOD SUGAR REGULATION. E. GEIGER and HILDE KROPF, Arch. f. exper. Path. u. Pharmakol. **139**:290, 1929.

Alimentary blood sugar curves were much lower after feeding oats than after a green fodder diet. Such curves were raised by the addition of acid to the green fodder diet, but lowered by the addition of alkali. The decreased sugar tolerance after a green fodder diet is not due to lack of glycogen in the liver. The increased sugar tolerance after an oats diet is decreased by the addition of acid to the diet.

KUGELMASS, New York.

EPIPHYSES AND LIVER EXTRACTS OF RATS FED ON CAROTINOIDS. BETH VON EULER, HANS VON EULER and P. KARRER, Biochem. Ztschr. **209**:240, 1929.

Normal growth is obtained in rats even in the absence of vitamin D if the diet contains 0.03 mg. of carotin per day. Furthermore, even with a sufficient amount of vitamin D the calcification was found to be defective unless carotin was also present in the diet. The presence of carotin or carotinoid was demonstrated in the liver extracts, provided the rats received not less than 0.03 mg. daily.

KUGELMASS, New York.

THE BEHAVIOR OF YOUNG AND OLD ANIMALS TOWARD ASPHYXIATION. M. REISS and F. HAUROWITZ, Klin. Wchnschr. **8**:743 (April 16) 1929.

Old mice succumb rapidly in an atmosphere of carbon monoxide, hydrogen or carbon dioxide. Young animals survive a long time under the same conditions. Old mice die rapidly from a lethal dose of strychnine or after their necks are placed in a clamp. Young mice live for a long time under these conditions. Ten

milligrams of hydrogen cyanide kills old mice in a few seconds. Young mice survive for eighty minutes. Chloroform kills mice with equal rapidity regardless of age.

KUGELMASS, New York.

PREPARATION OF A SUBSTANCE THAT REDUCES THE CALCIUM CONTENT AND ONE THAT REDUCES THE PHOSPHATE CONTENT OF SERUM: DEMONSTRATION IN THE SPLEEN AND IN THE LYMPH GLANDS. A. NITSCHKE, Klin. Wchnschr. **8**:794 (April 23) 1929.

It is possible, by suitable methods of extraction, to obtain a substance from the thymus gland which, when injected into animals, reduces the calcium content of the serum to an average of 7 mg. per hundred cubic centimeters, and leads to tetany and electrical hyperexcitability. Another substance can be isolated that has no effect upon the calcium but that reduces the phosphorous content of the serum by 50 per cent without producing systemic effects. Since extirpation of the thymus does not, regularly, lead to systemic effects, it was conjectured that certain other of the body glands may have a function similar to that of the thymus. This conjecture has been verified. Extracts have been prepared from spleen and lymph glands that are identical in properties with those described for thymus.

KUGELMASS, New York.

THE EFFECT OF CARBONIC ACID GAS MIXTURES ON THE RESPIRATION. A. VIETHEN and F. GRÜNEBERG, Klin. Wchnschr. **8**:887 (May 7) 1929.

Carbon dioxide, mixed with air or oxygen in concentrations of from 0.5 to 10 per cent, was administered in a series of thirty-one cases of pneumonia in children from 3 weeks to 14 years of age. The gas was given continuously in some cases and intermittently in others. In all cases an increased ventilation resulted. In carbon dioxide concentrations up to 4 per cent this increase was due entirely to a greater depth of respiration, resulting in as high as a 100 per cent increase in volume intake. With the higher concentrations there was also an increased rate of respiration. With a mixture of from 5 to 10 per cent the volume intake was as high as from 300 to 400 per cent above the previous intake. The results were the same whether oxygen or air was used in the mixture, and were unaffected by the age and weight of the child, the method of administration (continuous or interrupted) or the administration of a sedative. Under the conditions of the investigation the use of carbon dioxide gas as a therapeutic measure has no undesirable effects.

CRANE, Chicago.

THE TOXIC ACTION OF MILK AND OTHER SUBSTANCES EXPOSED TO ULTRAVIOLET IRRADIATION. P. REYHER and E. WALKHOFF, München. med. Wchnschr. **75**:1071 (June 22) 1928.

Mice and guinea-pigs were fed a normal diet and various substances which had been pretreated with ultraviolet rays. The substances included raw cow's milk, a dry milk, an egg yolk preparation, plasmon and ergosterol. All the animals showed pathologic changes of different types, degrees and duration. Nitrite-free raw milk contained nitrites after ultraviolet irradiation.

KUGELMASS, New York.

THE CHEMICAL REACTION OF VITAMINS. J. BULIR, Časop. lék. česk. **66**:1779 (Nov. 18) 1927.

A review of the literature on vitamins A, B, C, D and E is followed by a discussion of the saponification, heat resistance, solubility and other experimental reactions. The author states that vitamins A and C are prone to informative reactions, usually, but that biologic experimentation still gives the reaction of choice for determination of the presence of vitamins.

STULIK, Chicago.

SO-CALLED WATER INTOXICATION. HIROTADA MISAWA, Jap. J. M. Sc. **1**:355, 1927.

At intervals of thirty minutes, 50 cc. of tap water per kilogram of body weight was given to rabbits. This caused restlessness, polyuria, diarrhea, salivation, dyspnea and tremor. After about four hours, the water administered amounting to about one third of the total body weight, convulsions appeared. Blood tests at this time showed: a decrease in the dry substance to about 15 per cent; a decrease of 23.5 per cent in the serum protein, the protein quotient remaining unchanged; a reduction of chlorine, phosphorus, sodium, potassium, calcium and magnesium to about 20 per cent; a slight reduction in the residual nitrogen, hemoglobin and red cells; an increase in the blood sugar and white cells, and a percentage increase in the leukocytes. The animals were killed by bleeding, and the results of tests on the organs were compared with controls. The water content of all organs in the test animals was increased; the chlorine content was increased in the liver but decreased in all other organs, the greatest increase showing in the skeletal muscles. The urine chlorine, sodium, calcium, phosphorus and nitrogen were increased; the magnesium was unchanged and the potassium decreased. Further administration of water caused death. The body temperature decreased 2 degrees when convulsions appeared.

KUGELMASS, New York.

Nutrition

NUTRITIVE VALUE OF ICE-CREAM. L. S. PALMER, Am. J. Pub. Health **19**:601 (June) 1929.

Groups of rats were fed on (1) a basal diet, (2) this same diet mixed with one third its weight of ice cream and (3) an all ice cream diet. The ice cream contained 30 per cent of total solid and 12 per cent fat. The rate of growth of all these animals was considerably slower than that of animals fed the breeding diet; but by the end of ten months, group 2 had reached the same weight as the breeding animals. The animals of group 3 were still gaining at that time and eventually attained the full mature weight. The animals of group 1 ceased gaining when they attained one-half this weight. At the end of the ninety-day period, none of the animals in group 1 had attained the weight of the poorest animal fed the diet of group 2, although the mean consumption of the total nutrients was the same. Only one animal in group 1 attained the weight of the poorest animal of group 3. Dry matter consumed for each grain gained per hundred grams of body weight was 8.74 Gm. for group 1, 6.04 Gm. for group 2 and 5.44 Gm. for group 3.

KUGELMASS, New York.

THE ROENTGEN-RAY DIAGNOSIS OF INFANTILE SCURVY. RALPH S. BROMER, Am. J. Roentgenol. **19**:113 (Feb.) 1928.

The author summarizes the literature and makes a plea for unification of terminology because of the confusion of "white line," "Trummerfeld zone," and "scurvy line," which are used loosely by many authors. He then discusses the clinical manifestations, pathology, microscopic pathology, roentgenologic changes and differential diagnosis and gives an analysis of cases. The differentiation of coincident rickets, early osteomyelitis, sarcoma, osteochondritis luetica and periostitis luetica may be confusing. In fifty-six cases studied, the concentric ring about the epiphysis (Wimberger's sign) with a ground glass atrophy of the central portion was noted irrespective of the stage of the disease. Four roentgenographic stages are given: 1. An early or latent condition with a smooth, transparent ground glass appearance of the shaft, especially near the diaphyseal end, a thin cortex, and a broadened zone of temporary calcification at the very end of the shaft. 2. A well developed clinical condition with a zone of decreased density just behind the dense broadened zone of temporary calcification at the end of the diaphyseal

shadow, "the frame work marrow zone." Lateral spurs or projections at the diaphyseal end may form. 3. Well developed subperiosteal hemorrhages. The hemorrhagic effusions end abruptly at the diaphysis where the periosteum is firmly attached. Epiphyseal separation often takes place. 4. A healing stage with absorption of hemorrhage and repair of scorbutic lesions. The earliest disappearance observed roentgenographically was in one month, while in another case, signs remained after seventeen and one-half months. Periosteal thickening was found after five years. A bibliography is given.

STULIK, Chicago.

SOME OBSERVATIONS OF THE RESULTS FOLLOWING THE USE OF DRY MILK IN INFANT FEEDING EXTENDING OVER A PERIOD OF TEN YEARS. M. M. MCCORD, Arch. Pediat. **46**: 561 (Sept.) 1929.

The author has employed dried milk prepared by the Just roller process in feeding several thousand infants during the past ten years. He has obtained the best results from a 12 per cent dry milk. In most instances failure to take it was due to lack of cooperation on the part of the mother. The results from dry milk feeding have been all that one could desire. It is a safe method, there being no fear of bacterial contamination. The Just roller process of drying requires less than one minute and does not injure materially the antirachitic or the antiscorbutic properties of the milk. Dry milk is more digestible than liquid milk. All of the fat is utilized, in contrast to the fat of milk much higher in fats, in which it is not all utilized.

WILSON, Norfolk, Va.

GOAT'S MILK ANEMIA. C. M. HYLAND, Arch. Pediat. **46**:673 (Nov.) 1929.

The writer cites cases reported by three other authors, and he reports two cases of anemia in infants receiving goat's milk exclusively. The laboratory observations were those of rather severe secondary anemia, with low hemoglobin, low erythrocyte counts and rather marked evidence of blood regeneration. There was achromia, anisocytosis, poikilocytosis and basophilic degeneration. There were many macrocytes and microcytes; normoblasts and megaloblasts were also present.

WILSON, Norfolk, Va.

EXPERIMENTS ON NUTRITION: COMPARATIVE VITAMIN B VALUES OF FOODSTUFFS, PULSES AND NUTS. ROBERT H. A. PLIMMER, WILLIAM H. RAYMOND and JOHN LOWNDES, Biochem. J. **23**:546, 1929.

Material	Amount in Diet for Maintenance, Per Cent	Relative Vitamin B Value
Dried yeast	4	100
Split peas	30	13
Whole dried green peas	30	13
Lentils	30	13
Haricot beans	40	10
Soy beans	30	13
Peanuts	20	20
Ground almonds	40	10
Whole almonds	40	10
Hazelnuts	20	20
Coconut	No maintenance	0

KUGELMASS, New York.

THE CHILD WHO WILL NOT EAT. HENRY E. STAFFORD, California & West. Med. **32**:18 (Jan.) 1930.

Stafford gives the following suggestions to the parents of the child who will not eat: "1. That a well-prepared meal be offered at regular times. 2. That it be served in an appetizing manner. 3. That the child shall come to the table in

a proper mental attitude, e. g., free from fatigue. 4. That the child shall remain at the table uninterrupted for thirty minutes. 5. That no mention of food be made during or between meals."

DICKEY, San Francisco.

DETERMINATION OF VITAMINS A, B AND C IN COLLARDS AND TURNIP GREENS. G. W. BURTON, J. Home Economics **20**:35, 1928.

A quantitative study of the vitamin B content of turnip greens showed that 0.18 Gm. of raw greens was sufficient for the maintenance of rats over an eight week period or that 1 Gm. contained 1.25 units of vitamin B. With raw collards 0.9 Gm. was sufficient for the maintenance of rats over that period. Cooking turnip greens for thirty minutes in just sufficient water to take up the greens at the end of the period resulted in a 10 per cent loss of vitamin B. Similar cooking of collards for two hours resulted in from a 40 to a 50 per cent loss of vitamin B. No loss of vitamin A was noted. Five-tenths gram of raw collard and slightly over 1.0 Gm. of raw turnip greens contained enough vitamin C to protect rats against scurvy, while cooked collards the equivalent of 10 Gm. of raw collards did not contain sufficient vitamin C to protect guinea-pigs.

KUGELMASS, New York.

THE VITAMIN-A CONTENT OF AVOCADOS. LEROY S. WEATHERBY, J. ELLSWORTH YONTZ and RUTH V. WATSON, J. Home Economics **21**:360, 1929.

In feeding experiments on albino rats by a curative method, the Calavo grade of avocado which met the highest standard of maturity and oil content, was shown to be high in vitamin A. The quantity of avocado necessary to maintain an average growth of 3 Gm. per week during an eight week test period, the standard suggested by Sherman for the unit of vitamin A, would be considerably less than the smallest quantity used, 2.5 Gm. Based on the United States Pharmacopeia unit for vitamin A, the quantity of avocado required would be less than that required for the Sherman unit.

KUGELMASS, New York.

UTILIZATION OF FATTY OILS GIVEN PARENTERALLY. MARTHA KOEHNE and LAFAYETTE B. MENDEL, J. Nutrition **1**:399 (May) 1929.

Coconut, peanut butter and cod liver oils, when injected parenterally into albino rats and dogs, were utilized only to a slight degree if at all. The metabolism of the oils is extremely slow and is surely not a dependable source of energy to animals. Coconut oil was better tolerated than the rest and seemed to have a definite though sparing effect on protein catabolism. Starvation had little influence in forcing the utilization of oils by the experimental animals. Both vitamins A and D in cod liver oil can be utilized by young rats when administered parenterally; the vitamins of butter oil could not be so utilized. The dog is unable to utilize peanut oil. The utilization or nonutilization of fat-soluble vitamins A and D and of sudan III present in an oil at the time of its injection cannot be regarded as proof of the utilization or nonutilization of the oil which held it in solution. Fats administered parenterally are metabolized too slowly to exert a sufficient influence on nitrogen catabolism to make this method of evaluation practicable. A bibliography of forty-four references is appended.

KUGELMASS, New York.

THE SAFETY FACTOR OF PASTEURIZED MILK. H. C. CORRY MANN, Proc. Eighth World's Dairy Cong., 1928, p. 127.

Observations at the Evelina Hospital for children, at London, led to the following conclusions: 1. Milk that has been pasteurized by the low temperature holder process (145 F. for thirty minutes) is not damaged as food for infants. 2. No incidence of scurvy was observed over three years' time in children under

2 years of age who were given milk pasteurized at low temperature without a ration of orange juice; no increase in growth rate and no improvement in nutrition were noted from the addition of orange juice to a diet of milk pasteurized by this method. Experimental work extending over four years showed that a ration of pasteurized milk caused marked improvement in the nutrition of boys of school age when added to a basic diet that was poor in vitamins A, C and D. This indicated that the vitamin value of the raw milk was undamaged by pasteurization at a low temperature.

KUGELMASS, New York.

ACIDIFIED MILK FOR INFANT FEEDING. LEWIS THATCHER, Edinburgh M. J. **37**:37 (Jan.) 1930.

After a short review of the history of sour milk feeding, Thatcher gives his experience and opinion of the addition of lactic acid to cow's milk. The first investigation undertaken was the question as to whether acid added to milk inhibited the growth of bacteria. The conclusions reached were that no practical inhibitory effect was obtained, and that milk must always be guarded against contamination.

The explanation for the better handling of acidified milk by the infant lies in the production of finely precipitated casein lactate; in its effect on the p_H of the stomach contents, permitting a breaking down of the protein by pepsin and the later better action of the pancreatic enzymes; in whatever effect the maintenance of optimal gastric acidity may have in permitting the continuance of the other functions of the hydrochloric acid, such as bacterial destruction, pyloric regulation, activation of duodenal, pancreatic and biliary secretion and absorption of calcium.

Thatcher's method of preparation is somewhat different from that of Marriott and others in America. Certified milk is not boiled, but the cream is removed by skimming, leaving 1.75 per cent fat. As the child shows tolerance for fat, whole milk is gradually substituted. He believes "the benefit of giving unboiled milk is clear." Three drops of lactic acid are used for each ounce of food.

Normal infants and those with various ailments were fed with acidified milk. Some of the reports and charts are given in this paper. Thatcher believes lactic milk safe and satisfactory for infants of all ages. Sugar may be added in high percentage when needed. He believes that in certain acute conditions lactic acid milk cannot replace albumin milk.

NEFF, Kansas City, Mo.

IRRADIATED MILK IN RICKETS. MOURIQUAND, LEULIER and SCHOEN, Rev. de lait, February and March, 1928, nos. 72-73.

The authors discuss the use of irradiated milk and report the case of a girl, aged 20 months, showing marked rickets, who was treated during the period of twenty-three days with a liter of fresh irradiated milk a day. No other antirachitic treatment was given. At the end of this time, roentgenograms showed definite healing.

LESLIE, Evanston, Ill.

EXPERIMENTAL STUDIES ON THE EFFECT OF IRRADIATED ERGOSTEROL ADMINISTERED IN LARGE DOSES. BRUNO BORGHI, Biochim. e terap. sper. **16**:113 (April 30) 1929.

The experiments were made on normal and splenectomized rats. An injection of 10 mg. of irradiated ergosterol was given subcutaneously on alternate days for one month. On autopsy there was no evidence of any changes in the organs which would indicate a picture of hypervitaminosis (deposition of calcium on the walls of the vessels and in various organs). An occasional splenectomized animal showed a swelling of the myocardium and cells in the renal canaliculi. Borghi therefore inclines to the view that the toxicity observed after the administration of ergosterol was not due to the administration of vitamin D but to the presence of toxic substances associated with it.

KUGELMASS, New York.

THE AVOIDANCE OF NITROGEN LOSS IN FEVER BY FEEDING CARBOHYDRATE. OTTO BECK, Monatschr. f. Kinderh. **45**:498 (Jan.) 1930.

Knowing that carbohydrate spares protein and that there is a loss of protein during fever, the writer attempts to avoid this by the use of high amounts of carbohydrate. He ordered milk with 17 per cent sugar. This mixture unquestionably overcame the loss of nitrogen and permitted infants to gain during times when they ordinarily would have lost weight. One curve is of especial interest. The child had been exposed to measles. The high carbohydrate experiment was tried during the fever of vaccination. Following this a regular diet was ordered. Then the fever of the measles started. The weight curve and nitrogen excretion show a decided difference in the two feedings, the high carbohydrate feeding showing retention of nitrogen and gain in weight, and the low carbohydrate feeding the reverse.

GERSTLEY, Chicago.

SOME ORGAN ALTERATIONS BY LARGE DOSES OF VIOSTEROL IN THE RAT. F. HOLTZ and T. VON BRAND, Ztschr. f. physiol. Chem. **181**:227, 1929.

Viosterol, a vitamin D preparation, was dissolved in olive oil and fed to rats in doses as high as 100,000 times the therapeutic dose. The animals receiving this high dosage (19 mg. per day) made much smaller gains in weight than the control animals or those receiving 0.1 mg. Histologic examination of the organs showed calcification in the kidney, the lung and occasionally the aorta, but not in the heart, liver, spleen or suprarenals. These alterations may possibly be due not so much to hypervitaminosis as to chemical substances present in the preparation, since aldehydes, lactic acid, pyruvic acid, hydrogen peroxide and benzoyl peroxide are known to produce similar effects.

KUGELMASS, New York.

VITAMIN A. L. K. WOLFF, Nederl. tijdischr. v. geneesk. **2**:4465 (Sept. 28) 1929.

The author, who is the successor of Professor Eykman in Utrecht, first discusses the symptoms which occur when vitamin A is lacking in the diet: xerophthalmia, and keratomalacia are well known, and hemeralopia also may occur in men. Further, xerosis conjunctivae is not an independent condition but in other places of the body the epithelium may also show abnormal horn-formation. In animals dead from deficiency of vitamin A pus processes are frequently found at different places, showing decreased immunity against bacterial infection. Failure of vitamin A may further give rise to incrustations of the epithelium of the kidney and to stone formation in the kidney and the bladder.

Secondly, the question of the determination of vitamin A in food is discussed as to (1) therapeutic and prophylactic determination in animal experiments and (2) chemical determination with the reaction of Carr and Price. The author gives as his personal opinion that other fats than cod liver oil give this reaction. But sometimes it is necessary to concentrate the vitamin A as may be done by saponification. The nonsaponified part contains all the vitamin A.

It is not yet proved, that fats occur which contain vitamin A but which do not give the reaction.

A great disadvantage of the reaction is that it is also produced by some substances which do not have the properties of vitamin A (e. g., the so-called carotinoids and bixin). The carotinoids, however, do not give another test for vitamin A; phloroglucin and bixin may be excluded by saponification of the fat.

The foods which contain vitamin A are discussed; in the animal organism the liver contains the greater part by far.

Finally, the author discusses the question as to how much vitamin A is needed daily and how large the supply of vitamin A is in the liver of human beings and of animals. The average amount found by the author in the liver of the cow was 25 units per gram. The average amount in the human being, determined from the result of the investigation of 600 livers obtained at autopsy, was 17 units per

gram. In thirty-nine persons who had died by accident the average amount was 21.5 units; in persons dead from an acute disease, 20.7 units. In chronic disease less than 6 units of vitamin A per gram were found in the liver of 30.3 per cent of cases.

In many new-born infants the liver did not contain any vitamin A. No definite influence of the season could be found.

VAN CREVELD, Amsterdam, Holland.

FEEDING OF THE NORMAL AND SICK CHILD WITH KEFIR AND KEFIR SOUPS. K. ŠVEHLA, Časop. lék. česk. **66**:1241 (July 29) 1927.

Kefir is recommended because it keeps for periods over six years, it conserves the milk supply, it preserves its dieteticotherapeutic qualities and is not expensive. It is recommended for mixed feeding, artificial feeding and as an adjuvant to other artificial foods; the vitamin content makes it of value in replacing other vitamin preparations. Kefir soups with barley or rice water, flour and sugar were found valuable in selected cases. A vitamin soup was made by the addition of egg yolk and lemon juice. The acidity can be varied between 20 and 25 (Soxhlet-Henchel) by the fermentation period.

STULIK, Chicago.

THE MINERAL COMPOUNDS OF HUMAN MILK. OTAKAR LAXA, Časop. lék. česk. **66**:1792 (Nov. 18) 1927.

A complete chemical study of the ash, dialyzable and nondialyzable fractions of human milk was made. Comparative figures of other workers are cited. Human milk contains twice as much sodium chloride and almost three times as much potassium chloride as does cow's milk. On the other hand, human milk contains one third as much calcium phosphate, one half as much magnesium phosphate and a smaller amount of calcium citrate Calcium caseinate in human milk is two thirds as abundant as in cow's milk.

STULIK, Chicago.

SECRETIONS OF DIGESTIVE GLANDS AND BLOOD CHEMISTRY: I. ALKALI RESERVE AND CHLORIDES IN BLOOD. S. PRIKLADOWIZKY and M. BRESTKIN, Russ. J. Physiol. **11**:445, 1928.

Normal digestive activity causes a fluctuation in the alkali reserve depending on the kind of food taken. The alkali reserve is raised during the first two hours after feeding lean meat. It gradually returns to its initial value. It is also raised by feeding white bread. Feeding with fat causes a fall followed by a rise. Fluctuations of alkali reserve in the course of digestion are generally accompanied by inverse fluctuations of the chloride content of the blood.

KUGELMASS, New York.

GASTRIC LIPASE IN HEALTHY BABIES FED WITH MOTHER'S MILK. KUMATARO GONDO, Nagasaki J. Med. **6**:681, 1928.

The gastric lipase was measured by the Tona-Michaelis method with ten babies from 45 days to 1 year old. Gondo took into consideration the fact that the human milk has a marked lipase action while cow's milk has not. After milk is given, the lipase action increases with the lapse of time, but the individual variation is fairly large. Three hours after milk is given, the action is invariably intense and the individual variation is also small.

KUGELMASS, New York.

HYPERAVITAMINOSIS: I. STUDIES ON THE METABOLISM OF THE HYPERAVITAMINIZED RABBIT. H. SUGATA, Sei-I-Kwai M. J. **48**:1, 1929.

When an excess of vitamin A is injected into the rabbit, there is a gradual increase in blood nonprotein nitrogen, uric acid, creatinine and creatine and a

decrease in urea. The blood sugar shows a temporary rise followed by a drop in amount. The glycogen of the liver and the muscles decreases. The plasma lecithin and the fatty acids increase more than does cholesterol, while in controls receiving injections of cholesterol and olive oil or of cod liver oil there tends to be an increase in cholesterol instead of in lecithin. The animals show almost the same symptoms as when emaciated after vigorous exercise, and they die in a short time. With moderate doses of the vitamin there is a subcutaneous accumulation of fat and a decrease in urinary excretion, the two factors together causing an increase in body weight. There is a negative nitrogen balance, and a decrease in urea and an increase in ammonia excretion. These results furnish evidence that death caused by an excess of vitamin A is the result of destruction of cell activity, due to overfunction.

KUGELMASS, New York.

Prenatal Conditions

FETAL BACTEREMIA: A CONTRIBUTION TO THE MECHANISM OF INTRAUTERINE INFECTION AND THE PATHOGENESIS OF PLACENTITIS. ALFRED J. KOBAK, Am. J. Obst. & Gynec. **19**:299 (March) 1930.

Following a résumé of the literature, the author states his conclusions that led to the detailed study of 374 cultures of fetal blood drawn from the umbilical cord during the third stage of labor. In 9 per cent the results were positive; the placentae of this group were checked by histologic study for cellular reaction to inflammation and stained for bacterial invasion. Babies that died during this period of observation were also examined histologically and bacteriologically.

The invasion of fetal tissues is probably due to a placentitis caused by an ascending infection. This ascending infection is most common following prolonged rupture of the membranes. It may, however, occur with intact membranes, either extra-ovularly or perhaps through the maternal blood stream.

Only two of the babies showed outward effects of the bacteremia. One died in utero, revealing marked degeneration in all the tissues and multiple abscesses in the gums. In the other infant conjunctivitis (pneumococcic) developed, which presumably had as its focus an infection of the mother's ear with *Pneumococcus*.

ALLEN, Chicago.

CONGENITAL OBLITERATION OF THE BILE-DUCTS WITH A DESCRIPTION OF TWO CASES. LESLIE COLE and C. H. WHITTLE, Brit. J. Child. Dis. **26**:258 (Oct.-Dec.) 1929.

Postmortem observations in two male infants, aged 5 months and 8 weeks respectively, showed mixed multilobular and unilobular cirrhosis of the liver with biliary stasis, enlarged mesenteric and portal lymph nodes and inflammatory cells in the liver, and a tendency to hemorrhage evidenced by bleeding into the intestine and lungs. In one case the gallbladder and the common and cystic ducts were obliterated, whereas in the other the gallbladder was present but contained only mucus without bile and the common duct was present and patent as far as the duodenum.

The authors favor the theory that the original lesion is a congenital narrowing of the duct, with subsequent stagnation, irritation and inflammation.

The authors cite Ladd's report of several cases in which operation was followed by recovery. They state, however, that in the two cases described, operation would not have been possible.

LANGMANN, New York.

CHONDRODYSTROPHIA FOLLOWED BY NORMAL DEVELOPMENT. C. W. VINING, Proc. Roy. Soc. Med. **23**:112 (Dec.) 1929.

A case of chondrodystrophia was reported in a girl, aged 11. She was seen at 4½ years of age on account of backward development. She did not walk until she

was 4 years of age and did not talk until 4½ years. At that time, severe rickets, achondroplasia and cretinism were all considered, but the clinical picture was not typical of any one. The long bones were very short, and the feet very small. Treatment with cod liver oil emulsion and thyroid extract was begun. Improvement was rapid. When the child was 6 years of age, roentgenograms of her bones showed a normal appearance. At 9 years thyroid extract was discontinued. When the patient was last seen, at the age of 9 her mental condition was normal. Her mother stated that she was extremely active, well behaved and good tempered.

WILLIAMSON, New Orleans.

CONGENITAL ANOMALIES OF THE KIDNEY. H. SLOBOZIANO, P. HERSCOVICI and D. RAILEANO, Nourrisson **17**:350 (Nov.) 1929.

All of the anomalies recorded in this article occurred in monsters. The first was in a nosencephalus which was viable at birth but which died in a few hours. The right kidney was surrounded by a large cyst which was filled with a clear fluid. The kidney itself was small, weighing only 8 Gm. On section the kidney was found to be filled with small cysts. The left kidney presented a similar cystic condition. The suprarenal glands were absent.

In the second case, an infant was born prematurely with an encephalocystomeningocele. It died on the fifth day following an operation on the encephalocele. In addition to other defects the right kidney was large and had a dilated ureter containing a kink. The kidney and ureter on the left side were absent. The left suprarenal gland was hypertrophied.

The third infant was stillborn at the seventh month. It had a congenital hydronephrosis more marked on the left side. The ureters were dilated and bent. They did not have any demonstrable opening into the urinary bladder. No suprarenal glands were found. The mothers of two of these infants were syphilitic.

MCCLELLAND, Cleveland.

NOTES ON THE PROBLEM OF THE PREMATURE INFANT. E. ZELTNER, Gsndhtsfürs. f. d. Kindesalt. **4**:493, 1929.

The author reports a careful study of 240 premature infants which were under the care of the Infant's Home of the city of Nürenberg. The mortality is probably the lowest that has been published in a study of a large group. This is particularly remarkable in the class under 1,000 Gm. Zeltner records the astonishing mortality of 69 per cent; Ylppo's mortality for premature infants of the same weight was 94, and practically all other publications concur. The fact that 67 per cent of Zeltner's patients were admitted with temperature above 35 C. (95 F.) may in part explain his good results.

The infants were transferred to a special closed ward under the supervision of a special nurse. No visitors were allowed. Zeltner considers this the cause of his low number of infections: 2.8 infections per child per year. Apparently breast milk was used, but protein was added by the administration of one of the proprietary protein compounds, or by supplementing the breast milk with buttermilk or casein milk. Gavage was liberally used when indicated. The author found it impossible to secure a normal gain if the caloric index was below 120. Fever due to overheating was eliminated after the infants had been put in charge of a special nurse. Zeltner emphasizes the importance of nursing, and of assigning small number of children to each nurse.

The third week of life was an especially critical period, an observation that had also been made by other workers. On the other hand, the prompt care of the premature infant immediately after birth was a determining factor in the reduction of total mortality. Autopsy was performed on thirty-six of the forty-three patients who died. In only four cases was a hemorrhage found in the brain. There were four cases of sepsis, eleven of pneumonia and twelve of alimentary

disturbance. As other authors have also found, Zeltner sees no great difference between the development of premature and of full term infants after the first year. It is disappointing that in the entire article the author hardly mentions the extremely important factor of the prophylaxis of rickets.

REICHLE, Cleveland.

POSTERIOR ENCEPHALOCELE. CORNELIA DE LANGE, Jahrb. f. Kinderh. **126**:253 (Feb.) 1930.

The author gives a detailed report of gross and microscopic observations in a case of posterior encephalocele. Anomalies were present in all parts of the central nervous system. Extensive ependymitis in this case is considered to be of late origin. The essential developmental anomalies probably originated at a very much earlier period. Probably there was a familial factor: A cousin had a congenital anomaly of the kidneys; a brother, encephalocele, hydrocephalus, and polydactylism, and a sister, microcephaly, double cleft palate, cervical spina bifida and cystic kidneys. The patient described had also cleft palate, micrognathism and malformation of the external ear.

CLAUSEN, Rochester, N. Y.

ARACHNODACTYLIA. J. BROCK, Ztschr. f. Kinderh. **47**:702, 1929.

On the basis of an earlier and a later observation of the author on arachnodactylia, the latter occurring in a girl, aged 10, much retarded in growth, length and mentality, the pathogenesis of this anomaly of constitution is discussed. The characteristic stigma of spider fingers is traced back to the grand principle, occurring constantly in these children of marked habitus asthenicus, diminished growth and thickness of all tissues with undiminished growth in length. The difference between many cases of arachnodactylia and of status dysrysicus leads back to a genotypical correlation, as it returns again and again in different degenerative forms of habitus.

EMERSON, Boston.

TRIPLETS. CORNELIA DE LANGE, Nederl. tijdschr. v. geneesk. **2**:5678 (Dec. 7) 1929.

The author gives all her observations on triplets, three boys, during their first year of life. The first pecularity in their life was that each infant had its own placenta and its own chorion. Nearly always triplets comprise one single-ovum and one separate twin. In the first child, tetany developed within twenty-four hours after it had received treatment for pyelitis with potassium citrate (Thomson). The symptoms of tetany were present before the urine was alkaline. From this experience it follows that one should never give the Thomson treatment to a baby before being convinced that the child has no symptoms of latent spasmophilia.

When the second boy was about half a year of age, an arthritis of the left shoulder joint developed. The peculiarity was that puncture revealed pus that contained *Bacillus enteritidis* Gärtner, whereas the general condition was good and symptoms of enteritis were lacking.

The third boy had a slight hydrocephalus when he came into the hospital at the age of 9 months. The author discussed the relationship between the hydrocephalus and rickets.

VAN CREVELD, Amsterdam, Holland.

THE ORIGIN OF MALFORMATIONS, ESPECIALLY MICROCEPHALIA. H. C. JELGERSMA, Nederl. tijdschr. v. geneesk. **2**:5700 (Dec. 7) 1929.

In the author's opinion many anatomic peculiarities of microcephalic idiots can be considered as a sign of decreased fetation or of so-called propulsion. Contrary to the generally accepted opinion, microcephaly thus should be a condition that is more remote from the morphologic conditions of the fetus than normal, and

thus not a sign of retardation. This theory is worked out and an analogous explanation is given for several other malformations. Bolk's theory of fetation is accepted as guide.

VAN CREVELD, Amsterdam, Holland.

Diseases of the New-Born

CISTERN PUNCTURE IN THE NEWBORN. L. HOWARD SMITH, Am. J. Obst. & Gynec. **19**:374 (March) 1930.

This is a report of a series of 190 cistern punctures done on babies from 30 minutes to 6 days of age. None of these infants revealed any evidence of intracranial hemorrhage, birth injury or bleeding from elsewhere in the body. They had all been delivered under one obstetric regime.

The author found that although gross examination showed 83 per cent of the fluids to be clear and 16 per cent bloody, on microscopic examination only about one fourth were found free from blood. On repeated puncture, this blood invariably disappeared from the fluid within from two to four days.

From the obstetric standpoint it would seem that in the first rather than in the second stage of labor, the use of pituitary for induction and Gwathmey anesthesia resulted in a high incidence of bloody fluids.

ALLEN, Chicago.

THE RELATION BETWEEN WEIGHT AND FLUID INTAKE IN NEW-BORN INFANTS. DROSSEL, Arch. f. Kinderh. **88**:30 (July 12) 1929.

In 600 cases collected and studied, it was found that, on the average, infants of lighter weight than normal drank relatively more fluid than infants of greater weight than normal. The only exception was in small children of from 2,000 to 2,500 Gm. There was an apparent betterment of the weight curve in infants given Ringer's solution and dextrose instead of plain water.

SANFORD, Chicago.

Acute Infections

PREPARALYTIC POLIOMYELITIS: TREATMENT WITH CONVALESCENT SERUM. W. L. AYCOCK, E. H. LUTHER, C. F. MCKHANN, E. C. SMITH and S. D. KRAMER, J. Infect. Dis. **45**:175, 1929.

One hundred and sixteen patients with preparalytic poliomyelitis were treated with the serum of persons convalescing from poliomyelitis. The outcome in these cases, as measured by case fatality rate, percentage of cases in which no paralysis developed, percentage of cases in which paralysis of the two severe grades developed, as well as by the average amount of paralysis per case, is strikingly different from the outcome in untreated patients in the same outbreak. That this difference is not due in any great degree to the inclusion among the treated patients of patients with milder forms of the disease, which are ordinarily missed, by reason of diagnosis, is indicated by the close correspondence between the results in the state at large and in Watertown-Waltham, where there were increased opportunities for detecting milder forms of the disease and where a larger number of the patients were seen and treated. A relatively enormous number of missed cases must be assumed to have occurred in order to equalize the outcome in treated and untreated patients. A house-to-house canvass in one locality in which the disease was prevalent failed to disclose the occurrence of any number of missed cases. All treated patients presented typical signs and symptoms of preparalytic poliomyelitis. The subsequent occurrence of some paralysis in 61.2 per cent of the treated patients indicates that we were not dealing largely with a nonparalytic form of the disease. Twenty-three per cent of the cases in which no paralysis developed were of the so-called dromedary type, as compared with 26.8 per cent of the cases in which paralysis developed. As the dromedary phenomenon is peculiar to poliomyelitis,

this is regarded as an additional substantiation of the diagnosis in the group of cases in which no paralysis developed. Of 143 patients observed for suspected preparalytic poliomyelitis, who were excluded, the majority subsequently were found to be suffering from other conditions. In only eight cases could the suggestion of abortive (not preparalytic) poliomyelitis be considered.

AUTHORS' SUMMARY.

DISSOCIATION OF DIPLOCOCCUS FROM MEASLES. RUTH TUNNICLIFF, J. Infect. Dis. **45**:235, 1929.

As a result of aging strains of measles diplococci, two additional culture types have been obtained. The original colony is a small, smooth colony with a wide green zone (small S); the first variant is a large, smooth, less green colony with a narrow zone of partial hemolysis (large S); these two colonies in ascites plain agar are clear and smooth with regular edges; the second variant is a large, smooth, moist, slightly green colony with no hemolysis and is smooth, opaque and slightly granular on ascites agar (large SR). All forms are gram-positive. The original coccus is small, round or slightly elongated in pairs or chains; the first and second variants are large, round in pairs and clumps, the second variant often showing a capsule. The original small S culture does not ferment salicin; the two variants ferment salicin. The three culture types vary in their phagocytability, the original type is phagocytable, the first variant more so and the second variant generally not phagocytable. The small S type (Duval-Hibbard) now produces no substance toxic for paramecia, the large S type is slightly toxic and the large SR is very toxic for paramecia. The toxin from the large S type is partially neutralized by antimeasles-diplococcus goat serum and the serum of patients convalescing from measles; the toxin from the large SR type is neutralized by neither. By transplanting the three types twenty-one times in anaerobic blood agar cultures at 36 C., the small S type remained the same; the large S colonies were changed to SR, and the large SR to large S colonies, but small S colonies appear in neither the large S nor the large SR cultures. By transplanting the large S and the large SR cultures frequently in dextrose broth at room temperature or at 36 C., the large S could be changed to large SR and SR to large S colonies, but only after twenty-five transfers in dextrose broth at room temperature did the large S type revert to the small, smooth colony with a wide green zone (small S).

AUTHOR'S SUMMARY.

A STUDY OF RHEUMATIC DISEASE IN CHILDREN. MAURICE CAMPBELL and E. C. WARNER, Lancet **1**:61 (Jan. 11) 1930.

Rheumatic disease is now receiving the attention it deserves as the most crippling disease of the children of the poor; 15 per cent of these above the age of 3 who come to two hospitals in London have this disease.

In 250 cases, three girls are affected for every two boys. The commonest age for onset was found to be 6 or 7 years. There was a family history of rheumatism in nearly 60 per cent, but in only 20 per cent of nonrheumatic controls.

One of the most important factors predisposing to rheumatism is debility. Thus, an attack often follows measles or scarlet fever. Tonsillitis may predispose to rheumatism. There is almost always a latent period of from several days to three or four weeks.

Permanent signs of heart disease remained in 15 per cent of the "out-patients" and in 30 per cent of the "in-patients."

Complete enucleation of the tonsils before there were any signs or symptoms of rheumatism (on an average, two years before) did not prevent its onset or diminish its frequency, nor did it in any way lessen the incidence of rheumatic carditis. The only justification for the removal of the tonsils in a rheumatic child is undermining of the general health by repeated sore throats or by very septic tonsils.

LANGMANN, New York.

THE ASCHOFF NODULE IN RHEUMATIC PNEUMONIA. A. D. FRASER, Lancet **1**:70 (Jan. 11) 1930.

A woman, aged 20, was admitted to the hospital with painful, swollen joints and pain in the chest. Pericarditis with effusion and bilateral pneumonia developed, and she died on the eleventh day after admission. Autopsy revealed many Aschoff nodules in the myocardium, rheumatic pericarditis and endocarditis of the mitral and aortic valves. The lungs showed acute interstitial pneumonia with collections of endothelial cells in the interstitial tissue, some of them large and multinucleated surrounding necrotic collagen fibrils which the author interpreted as "typical Aschoff nodules."

In a second case, a boy, aged 15, was admitted with the diagnosis of meningitis; he died two hours after admission. Autopsy also revealed typical acute rheumatic endocarditis of mitral and aortic valves but no Aschoff nodules in the myocardium and no evidence of pericarditis. The lungs showed a picture similar to that in the first case.

LANGMANN, New York.

EXPERIENCES WITH THE DICK TEST. TARO TOYODA, JOJI MORIWAKI and YASUO FUTAGI, Lancet **1**:73 (Jan. 11) 1930.

The following data were obtained in the Japanese Isolation Hospital, Dairen, Manchuria: Of 11,284 healthy Japanese, 37.2 per cent gave a positive reaction to the Dick test. Female subjects showed a higher positive rate than did male. In 305 cases of scarlet fever, 41 cases (14 per cent) occurred in persons with a negative reaction to the Dick test. Generally speaking, the more intense the Dick reactions the more severe the case and the higher the percentage of complications.

The authors conclude that the Dick test is a reliable indicator of susceptibility to scarlet fever, the only exception being in those cases in which an allergic response develops to the heat stable constituent of Dick toxin.

From the standpoint of immunization, Dick toxin partakes much of the nature of heat labile toxin. When a course of injections of heat stable toxin is given, either there is no effect on the skin reaction to Dick toxin or an allergic skin response develops. No allergic reaction to Dick toxin appears to be produced after immunization with pure heat labile toxin.

LANGMANN, New York.

SCARLET FEVER AND ANGINA. I. L. RISKIN, München. med. Wchnschr. **76**:1913 (Nov. 15) 1929.

Riskin found many points of similarity between scarlet fever and angina. In persons who are in contact with patients having scarlet fever angina frequently develops and, vice versa, scarlet fever often develops in persons in contact with those having angina. An investigation was made on 222 nurses and mothers who were taking care of patients with scarlet fever at a hospital for contagious diseases. Eighty-seven developed angina in the hospital and twenty-two had an attack of angina at home before scarlet fever developed in some one else in the family. The time between exposure to scarlet fever and the appearance of angina was between four and nine days in the majority of cases, with extremes of one and sixteen days. Twenty-seven of the 222 nurses had had scarlet fever in childhood; seventeen of these developed angina. There was no relation between the reaction to the Dick test and the occurrence of angina.

BRAHDY, Mt. Vernon, N. Y.

BACTERIOLOGIC EXAMINATION OF SCARLET FEVER STREPTOCOCCI. E. FAUVET, München. med. Wchnschr. **76**:2048 (Dec. 6) 1929.

The best culture medium for scarlet fever streptococci is still an unsettled problem. Fauvet found agar containing 5 per cent freshly drawn human blood

superior to agar containing the same amount of defibrinated sheep's blood as described by Dold and Müller. In addition, the author found that in 268 cultures from both the nose and the throat there were fourteen instances in which the culture from the nose was positive when the culture from the throat was negative. For this reason he urges that cultures be taken from the nose as well as the throat in all cases.

BRAHDY, Mt. Vernon, N. Y.

A CONDITION FAVORING THE DEVELOPMENT OF ENCEPHALITIS POSTVACCINATIONEM. O. REISCH, Wien. klin. Wchnschr. **43**:103 (Jan. 23) 1930.

The author has observed two fatal cases of postvaccinal encephalitis, showing the characteristic histologic picture described by Lucksch and Turnbull. During life, these patients had myoclonia affecting most of the voluntary muscles. Six other cases were studied in detail. A careful investigation of about 300 children in the same neighborhood revealed the presence of myoclonia in many and in both the vaccinated and unvaccinated children to an equal extent. The author believes that he is observing an epidemic of disease that may become a serious menace to those who have been vaccinated.

CLAUSEN, Rochester, N. Y.

DISAPPOINTMENTS IN SERUM THERAPY. P. H. KRAMER, Nederl. Tijdschr. v. Geneesk. **2**:4111 (Sept. 7) 1929.

In this article the author discusses serum treatment in some diseases. In tetanus serum treatment has great value as a prophylactic, but the therapeutic value is small when symptoms of the disease have already appeared.

In epidemic meningitis the serum treatment has resulted in many failures. The author does not give any more intralumbar injections of the serum. How much of this discrediting of the serum therapy is due to other factors, among which the author mentions especially an increased virulence or a modification in the character of the meningococcus, cannot be said with certainty. Next to these "biologic" changes there exist "anatomic" difficulties which may explain the bad result of the serum treatment, especially of the intralumbar injection. The process of inflammation can modify the anatomic conditions so that the serum that is injected in the lumbar region, cannot reach the meningococci in the ventricles. The literature on this part of the problem is discussed, and especially the investigations of the late Sicard.

In diphtheria the serum treatment has given many failures in recent years. The severe toxic symptoms of diphtheria, whether they appear early or late, are occurring much more frequently and the serum has only slight influence on these cases. The increased mortality of diphtheria must be ascribed to this severe toxicity. However, this increase has not been so great in Holland as, for example, in Berlin. After the first months of 1929, the mortality decreased in Holland.

The question as to how far a coinfection, especially with streptococci influences the more malignant course of many cases of diphtheria of late years is raised and is answered in the negative.

The author gives as his opinion that the increase in the number of toxic cases of diphtheria which react unfavorably to sufficient quantities of serum given early is caused by a large production of virulent toxin.

VAN CREVELD, Amsterdam, Holland.

Chronic Infections

SINUSITIS AND TUBERCULOSIS IN CHILDREN. HENRY A. REISMAN, Arch. Pediat. **46**:667 (Nov.) 1929.

The author thinks it reasonable to suppose that sinusitis as a complication of infection of the upper respiratory tract occurs as frequently as otitis media. Cases of sinus infection should be regarded as potential cases of disease of the chest.

The lungs become involved either by way of the lymphatics through the submaxillary nodes, the retropharyngeal nodes, the deep cervical and internal jugular nodes, the great veins, the right side of the heart and the pulmonary artery or directly by inhalation.

Children with physical signs in the chest suggesting juvenile tuberculosis and with persistent negative reactions to tests for tuberculosis were found to have sinus infection. Improvement in the condition of the chest was prompt when remedial measures were applied to the sinuses. Thirty cases of pulmonary infections secondary to sinusitis were observed. The physical signs in the chest are almost identical in the early tuberculous and early nontuberculous cases. Frequently there is nothing suggesting sinus infection. The tuberculin test is of great value in differentiating the types.

Sinusitis is a great problem in children because it may simulate tuberculosis or aggravate it. When tuberculosis is present, not all cases of sinusitis show pulmonary changes.

WILSON, Norfolk, Va.

TUBERCULOSIS CLINIC FOR CHILDREN. LLOYD B. DICKEY, California & West. Med. **32**:90 (Feb.) 1930.

The work in a tuberculosis clinic for children is outlined. During the course of three years, about 2,500 children were examined for tuberculosis; 700 of these were found to be infected. There were 396 cases diagnosed as latent tuberculosis; the remaining patients were either suspected or proved to have various types of active tuberculous disease.

DICKEY, San Francisco,

ROENTGENOGRAMS OF CHILDREN VACCINATED WITH B.C.G. L. SAYÉ, Presse méd. **37**:1477 (Nov. 13) 1929.

Six hundred and four infants have been vaccinated at the University of Barcelona since 1924. Roentgenograms were taken of patients exposed to tuberculosis, and in control cases of those exposed under the same conditions but who had not had the vaccine. Others were taken of vaccinated patients who were in a normal condition. There was some evidence of lymphatic enlargement in the normal infants. Of the patients exposed to tuberculosis 5.1 per cent showed lesions that might be considered grave as compared with 42.4 per cent in patients who were not protected by the vaccine.

SANFORD, Chicago.

ANTITUBERCULOSIS CAMPAIGN IN BUENOS AIRES, 1928. ALEJANDRO RAIMONDI, Bol. Inst. internac. am. de protec. inf. **3**:225 (Oct.) 1929.

In relation to the child the antituberculosis campaign consists in: (1) the placement of new-born children of tuberculous parents, (2) vaccination with B. C. G., and (3) care in the Manuel Rocca Preventorium and in a seaside colony at Necochea.

In the last few years, the death rate for the 365 placed children has been about 30 per cent. In a group of 244 placed infants given B. C. G., the death rate was 19.7 per cent. In another unvaccinated group of 121, 32.2 per cent died. The children in the preventorium and the seaside colony made good progress.

LESLIE, Evanston, Ill.

IMMUNIZATION OF CATTLE AND SHEEP BY MEANS OF B.C.G. B. LANGE and R. WETHMAR, Ztschr. f. Hyg. u. Infekionskrankh. **110**:465, 1929.

The authors state that in their experimental animals the oral and subcutaneous administration of large doses of B.C.G. was never followed by progressive tuberculosis. The subcutaneous introduction caused a stronger and more lasting hypersensitiveness to tuberculin than the feeding of large amounts of bacilli. The

specific hypersensitiveness is not necessarily associated with an increased resistance to infection. After oral administration the animals were not sufficiently protected, even against intravenous inoculation with a very weak virus. The subcutaneous treatment also was insufficient in part of the animals in spite of a relatively weak test infection. In the majority of the animals the treatment was successful to some extent. Two of three calves and four of six sheep overcame the intravenous mild infection which for control animals was surely fatal. These animals, however, were not free from tuberculosis. When they were slaughtered in good general condition several months later, they all had limited but still active lesions. When a more virulent intravenous test infection was used, the animals did not show any specific protection. It is evident that in cattle and sheep the protection possible by means of B.C.G. is limited; in fact, the authors show that it is appreciably less than after intravenous injection of human tubercle bacilli.

OPHÜLS, San Francisco.

Internal Diseases

SEVERE SECONDARY ANEMIA DUE TO DIET. WILLIAM WILLIS ANDERSON, Arch. Pediat. **46**:712 (Nov.) 1929.

A twin boy, aged 16 months, that weighed 6¼ pounds (3 Kg.) at birth and 16½ pounds (7.2 Kg.) when seen, was the victim of a severe secondary anemia. He was nursed for two months and was then fed a mixture of sweetened condensed milk until 15 months of age.

A liberal diet was then prescribed, but his appetite was poor and he did not thrive. Following two intraperitoneal transfusions of whole blood he improved steadily; when seen a year later, he weighed 27 pounds (12.2 Kg.) and appeared to be well and as fully developed as his twin brother except that he was one-half inch (1.27 cm.) shorter.

WILSON, Norfolk, Va.

THE PATHOGENESIS OF GLOMERULAR NEPHRITIS. WARFIELD T. LONGCOPE, Bull. Johns Hopkins Hosp. **45**:335 (Dec.) 1929.

Longcope summarizes our present knowledge of the etiology and natural history of acute glomerular nephritis. He recognizes two types: the focal and the diffuse. "The focal form occurs during acute infections, and in the embolic type is usually ascribed to the deposition of bacteria in the capillary loops of the glomeruli where they lead to a necrosis, or to an inflammatory reaction. The diffuse form follows acute infections, proven to be due in such a large proportion of instances to hemolytic streptococci, that for the present it is justifiable to consider at least one variety of acute glomerular nephritis as a manifestation of streptococcic infection. In view of the great frequency of acute streptococcic infections, it must be considered as a rare manifestation. It cannot be proved that acute glomerular nephritis depends upon infection by a particular form of streptococcus, or upon the invasion of the blood or the involvement of the kidney by streptococci. There is some evidence, however, which indicates that patients suffering from acute nephritis are abnormally susceptible to the products of the growth of hemolytic streptococci; and it seems possible that some altered reaction of the tissues, such as occurs in allergy, or some unusual antibody response to the infection is the determining factor in the development of acute glomerular nephritis in individual cases. Permanent recovery is apparently more common in children than in adults. We have no observations to explain the difference. In a small number of adults we have found that recovery has followed elimination of the infection and the infecting organism, while progression of the disease has been coincidental with the persistence or the recurrence of hemolytic streptococcus infections. It further appears evident that there are instances of Bright's disease that run their entire course as progressive or recurrent diffuse

inflammatory glomerulitis, without involvement of the renal arteries or arterioles, and with changes in the renal tubules that may be regarded as secondary to the glomerular lesion and to the diffuse inflammatory reaction of the interstitial tissue. As a working hypothesis, therefore, we would suggest that it may be possible to differentiate, as one form of Bright's disease, a primary and specific glomerular nephritis which is to be interpreted probably as a manifestation of streptococcus infections in individuals who may be allergic to the streptococcus or its products of growth, or who possess some other peculiar form of tissue response to a local streptococcic infection."

LYTTLE, New York.

BRONCHOPNEUMONIA IN EARLY CHILDHOOD: ITS TREATMENT. E. P. COOK, California & West. Med. **32**:170 (March) 1930.

The systematic treatment for bronchopneumonia is outlined. The prophylaxis and the nursing care are emphasized. The important items in the nursing care are: temperature readings, ventilation, medicated air, diet, care of the bowels, counter-irritants, hydrotherapy and treatment for abdominal distention. Drug therapy should be used only symptomatically for cough, rest and sleep, cyanosis, circulatory and respiratory failure. Blood transfusions are of value in certain cases. The complications to be watched for, and to be treated when they occur, are dehydration, otitis media, pyelitis, empyema, meningitis and meningismus. The treatment during convalescence is important.

DICKEY, San Francisco.

OBESITY AS A PRECURSOR OF DIABETES. S. FRANKLIN ADAMS, J. Nutrition **1**:339 (March) 1929.

From the histories of 673 cases largely from rural districts, it was found that 91 per cent of the patients were overweight and that 82.9 per cent were more than 10 per cent overweight when the diabetes began. As age increases to the fifth decade, the persons in whom diabetes develops increase in weight; after the age 50, the percentage overweight is slightly lower. Obesity may be an important factor in young persons, because more than 30 per cent of persons less than 20 years of age were more than 10 per cent overweight before diabetes began. Diabetes appears to be associated with an excessive amount of total intake rather than with the amount of carbohydrates.

KUGELMASS, New York.

THE TREATMENT OF RHEUMATIC CARDIOVASCULAR DISEASE IN CHILDREN. WILLIAM D. STROUD, M. Clin. North America **13**:845 (Jan.) 1930.

This is a report on the condition of 272 children discharged from the Children's Heart Hospital of Philadelphia during a six year period. The following requirements for admission to the institution prevail. Patients shall have either possible or potential cardiovascular disease. None is admitted who has had congestive circulatory failure or for whom a hopeless prognosis has been given. Each child shall spend two weeks in a hospital before admission. So far as possible, all foci of infection must be removed. Parents shall permit the child to remain from three to six months. Treatment is confined entirely to rest, with salicylates in the acute arthritic (exudative) and pancarditic (proliferative) stages, followed by prolonged rest, with nourishing food, fresh air and sunshine in the subacute or more or less latent stages. Estimation of progress is based on the following criteria: the temperature, leukocyte count, gain in weight and general clinical picture. The average stay in the hospital is about six months. Of the 272 children discharged, 57 were dead at the end of the six year period, and 27 were not found; 144 (53 per cent) were attending school or working, and 44 were unable to attend school. This group of discharged patients represents children with heart disease of all degrees of seriousness. There seemed to be little

difference in the physical condition of children under and those over 10 years of age. Boys made a decidedly better showing than girls.

This report is offered as a possible basis for comparison with the results obtained with similar patients treated by serum vaccines and by "intravenous desensitization or immunization with suitable antigenic substances" now in the process of development.

SMITH, Ogden, Utah.

CHRONIC MUCOUS GASTRITIS WITH LOSS OF APPETITE IN CHILDREN. CHARLES GILMORE KERLEY, M. J. & Rec. **131**:23 (Jan. 1) 1930.

The patient suffering from loss of appetite is generally found in well-to-do families and is the only child in the family. Parents and nurses urge and coax the child to take a certain amount of food regardless of his desire. Directly these patients say they have had sufficient food they should not be given any more until the next meal. With loss of appetite there is often the complaint of nausea or of pain before meals, or in a few cases after meals. Constipation is usually associated with anorexia. The patient is somewhat underweight and habitually irritable; he sleeps poorly, and is not agreeable. A complete examination should be made, including a gastric analysis. A gastric analysis always shows a high total hyperacidity. The author discusses a plan for feeding these children, and also mentions drugs that may be of assistance. When test meals were given, the observer was impressed with the amount of food remaining in the stomach four, five or more hours after the completion of previous feeding. Mucus which floats in the water used in stomach lavage can be easily measured; not infrequently, as much as 2 ounces (59.1 cc.) is removed. If repeated lavage shows a continuation of food retention, skimmed milk should be used and butter and cream omitted entirely from the diet. Butter fat is unquestionably a retarding factor in the emptying process.

WILLIAMSON, New Orleans.

THE CHILD IN THE RHEUMATIC MÊLÉE. J. EPSTEIN, M. J. & Rec. **131**:26 (Jan. 1) 1930.

Much has been written on rheumatism but only slight progress has been made in its etiology, prevention and treatment. The rheumatic syndrome may manifest itself by various symptoms and signs. Not all aches and pains are rheumatic. The prevention of rheumatism involves the prevention of bad weather, unhygienic surroundings and ill health. During the acute stage, sodium salicylate should be given in moderate repeated doses till all symptoms and signs have subsided. After the acute attack the salicylate should be given periodically. The addition of sodium benzoate to the salicylate enhances its therapeutic value. Very large doses of salicylate are injurious. Salicylism does not cure rheumatism.

WILLIAMSON, New Orleans.

REPORT OF A CASE OF ACUTE PYELITIS IN INFANCY TREATED WITH PITUITARY EXTRACT. NATHAN GINSBERG, M. J. & Rec. **131**:28 (Jan. 1) 1930.

A child, aged 2 years, had been suffering from pyelitis for twenty-six days. The temperature ranged from 102 to 106 F. All the usual methods of treatment had been tried in vain. The author then gave an injection of 3 minims (0.18 cc.) of pituitary extract; after fifteen minutes, the temperature dropped from 106 to 100 F., but rose again in six hours. A similar dose was repeated and the temperature dropped again. Then the extract was given every two hours hypodermically in doses of 2 minims (0.12 cc.). The treatment was followed by a continued normal temperature and an uneventful convalescence.

WILLIAMSON, New Orleans.

OBSTRUCTION OF THE ŒSOPHAGUS IN CHILDHOOD. WILFRID SHELDON and A. G. OGILVIE, Arch. Dis. Childhood **4**:347 (Dec.) 1929.

Six cases were observed and the records of six additional cases were studied. Ten of the children had obstruction at the level of the seventh thoracic vertebra. In two the obstruction was at the level of the diaphragm. Ten of the patients were males. In all cases the symptoms began during the first year of life. These were vomiting of undigested food, constipation and malnutrition. The pathology is considered to be a recurring spasm of congenital origin. The most effective treatment is a fluid diet. The passage of bougies is contraindicated.

PETERMAN, Milwaukee.

REMOTE PROGNOSIS OF PNEUMONIA. H. P. JAMESON, Arch. Dis. Childhood **4**: 365 (Dec.) 1929.

Two hundred children who recovered from pneumonia were examined from one to ten years later. Physical examinations were made and roentgenograms of 101 patients were studied; fourteen patients showed a well marked pulmonary fibrosis; 58 children were examined who had had in the last ten years pneumonia which lasted more than three weeks. Three patients without symptoms showed diminished expansion, impaired resonance and weaker breath sounds over the affected area. Two showed signs over the same lung. Thirty-three of these patients were examined roentgenographically; nineteen showed some signs. Eighteen of the fifty-eight children showed severe symptoms of pulmonary catarrh. The remote prognosis of pneumonia depends on the amount, duration and recurrence of the interstitial inflammation, and also on the number of attacks which the child suffers.

PETERMAN, Milwaukee.

METABOLIC STUDY OF AN ALKAPTONURIC INFANT. FRANCES BRAID and EVELYN M. HICKMANS, Arch. Dis. Childhood **4**:389 (Dec.) 1929.

Metabolism studies, especially on the nitrogen partition, were made on a male infant, aged 4 months, with alkaptonuria. The complete protein metabolism was studied during four periods. In health on a milk diet the ratio of homogentisic acid to nitrogen is 55-60: 100, supporting the theory of a "maximal error." A fall in nitrogen retention was associated with a fall in the ratio to 34: 100. After thirty hours of starvation the alkaptonuria disappeared. Administration of potassium iodide by mouth had no effect on the output. There was a low urea nitrogen excretion. The total nitrogen absorption and retention were normal. The acidity of the urine was slightly higher than normal.

PETERMAN, Milwaukee.

CELIAC DISEASE. A. B. MARFAN, Nourrisson **17**:321 (Nov.) 1929.

This disease seems to be of rare occurrence in France. A review of the literature reveals its greater frequency in England and America. The marked disturbance in the digestion of fat is accompanied by lesser disturbances in the digestion of the carbohydrates and proteins. Studies on the digestive secretions and a postmortem examination of the digestive organs have shown no constant abnormalities. One of the author's patients had a positive Wassermann reaction and improved with antisyphilitic therapy. The usual dietetic therapy, including the use of bananas, is endorsed. Ultraviolet radiations are also recommended. Two cases are described in detail.

MCCLELLAND, Cleveland.

SECONDARY INFECTIONS OF THE GASTRO-INTESTINAL TRACT. A. B. MARFAN, Paris méd. **19**:394 (Nov. 2) 1929.

Marfan points out that diarrhea is simply the elimination of substances through the gastro-intestinal tract and may be due to bacteria, their toxins, and mineral

and vegetable poisons besides those in food. The principal causes of secondary diarrheas are in the acute infections, scarlet fever, diphtheria, smallpox, pneumonia and pyogenic organisms. In the chronic conditions, it is most often due to tuberculosis or to syphilis. As a point of diagnosis, a persistent high fever in an infant accompanied by diarrhea is almost never due to the diarrhea. A further point is the time of the appearance of the fever. If it comes on after the diarrhea has occurred, it might be due to a dehydration, but if it appears before, or coincidental with the diarrhea, the gastro-intestinal disturbance is usually secondary.

SANFORD, Chicago.

EDEMAS OF INFANCY. J. CATHALA, Paris méd. **19**:402 (Nov. 2) 1929.

Of the congenital causes of edema only two are of importance: congenital anasarca associated with hydramnios, and that associated with erythroblastosis of the liver. In the new-born are found physiologic edema or scleredema, generalized anasarca, edema due to debility or chilling, and that due to renal disturbances. In infants, disturbances of the renal function are the most frequent cause, and produce the so-called idiopathic edemas. The idiopathic forms may be divided into first those due to malnutrition. These comprise athrepsia and dehydration. The second type is due to constitutional and diathesic states, and the third to faulty feeding. In this group the principal food elements found at fault are: hypermineralization, forced carbohydrates, poor equilibrium between proteins and fats, and avitaminosis.

SANFORD, Chicago.

THE ETIOLOGY OF CERVICAL RIB. J. A. MATHEZ, Presse méd. **38**:67 (Jan. 15) 1930.

Mathez believes that the different osteal proliferations, such as Schlatter's disease and Koehler's disease, may be due to a subacute osteomyelitis, but that rickets may be a causative factor of cervical rib, as well as kyphosis. He cites a case in which a cervical rib was demonstrated in a case of rachitic osteomalacia which was successfully healed under treatment with irradiated ergosterol.

SANFORD, Chicago.

ANOREXIA IN CHILDREN: ITS CAUSE AND TREATMENT. LEREBOULLET, Progrès méd. **45**:418 (March 8) 1930.

Anorexias in children may be divided into four groups. In the first is anorexia from a general low state of nutrition, among these are found chronic eczemas, spasmophilias and nervous children. Anorexias in congenital syphilis, and tuberculosis are also placed in this group. The second type comprises the digestive disturbances; the third, local causes, such as pharyngitis, dentition and food served too warm, and the fourth those due to nervous conditions, including the mental elements. After treatment for the condition of which anorexia is a symptom, tonics are given, such as Vichy water, alkalis, peptones, thyroid and biliary stimulants. Ultraviolet therapy and irradiated ergosterol also are of great value.

SANFORD, Chicago.

LYMPHOSARCOMA OF THE RETROPERITONEAL GLANDS WITH MULTIPLE METASTASES IN AN INFANT AGED 6 MONTHS. LUCIEN GAROT, Rev. franç. de pédiat. **5**:491 (Aug.) 1929.

Enlargement of the abdomen was noted in this case from birth, but it became much more marked at the age of 4 months. At that time the nutrition of the child became markedly impaired. On the infant's admission to the hospital the thorax was also enlarged at the base and the respiratory movements were rapid

and feeble. Edema of the lower extremities developed after three days and progressed upward. At autopsy large masses of lymphosarcomatous tissue were found to occupy the dorsal portions of the abdomen; there were metastases in the liver.

LESLIE, Evanston, Ill.

"SYNDROME DU VENT DU MIDI," THÈSE DE LYON, 1929. ROGER CHARPENTIER.

This study was undertaken with the idea that there might be some factor in the meteorologic conditions accompanying the "vent du midi" (south wind) which would account for certain disturbances in infants which are seen at that time. The syndrome of the "vent du midi" is characterized by dehydration. In the severe state the child lies inert, the mouth open, the tongue dry, the fontanel sunken and the respiration difficult. Occasionally there is vomiting and diarrhea but not enough to account for the dehydration. Frequently the patients die. The atmospheric changes which accompany the "vent du midi" consist in a slight elevation in temperature and a slight lowering of the barometric pressure, but a marked lowering of humidity during the day and an absence of the usual nocturnal rise in humidity. Correlating this with the symptoms it seems probable that in this medium of dry air, the infant with its relatively large surface area loses large quantities of water by way of the skin and the lungs; the hypotrophic infant, which at best is hydrolabile, is among those most seriously affected. In substantiation of this supposition, no unfavorable effects are seen when rain accompanies the south wind.

LESLIE, Evanston, Ill.

A CASE OF SICKLE CELL ANEMIA IN A CUBAN CHILD. A. CASTELLANO, Bol. Soc. cubana de pediat. **1**:596 (Nov.) 1929.

The author reports a case of sickle cell anemia in a negro child, aged 1 year. Hemoglobin was 45 per cent and the red cells 2,720,000, with marked sickle forms. The treatment consisted in transfusions of whole blood. The recovery was rapid, the red cell count reaching 4,000,000 in sixty days. The author reviews the literature and discusses the possible etiology, especial attention being drawn to the hepatic functions as shown by the hemolysis in the van den Bergh test.

SANFORD, Chicago.

PULMONARY SUPPURATIONS IN INFANCY. A. ABALLI, Bol. Soc. cubana de pediat. **1**:650 (Dec.) 1929.

Thirteen cases of bronchietasis and pulmonary abscess are presented, in which the age of the patient varied form 3 months to 11 years. Complete roentgenograms are given. The author concludes that these conditions are most often confused with lobar pneumonia or bronchopneumonias or their secondary pleural reactions. Roentgenograms are the only assured means of diagnosis. These should always be taken in disturbances of the lung in children, and the number of cases in which the diagnosis of abscess of the lung will rise accordingly. Bronchoscopy offers the only method of treatment.

SANFORD, Chicago.

THE TREATMENT FOR PNEUMONIA IN INFANCY BY BILE SALTS. A. CASTELLANOS, Bol. Soc. cubana de pediat. **2**:32 (Jan.) 1930.

Biliary salts show a selective action in the lysis of pneumococci and are rapidly eliminated. The taurocholate is better then the glycocholate in this respect. There is enough margin between the lytic dose and a pathologic reaction for the host to make this method practicable for clinical purposes. The therapeutic dose is 5 cc. per kilogram of body weight. It is best to type the organism, as type III pneumococcus requires the addition of magnesium sulphate to the bile salt solution to make this effective. This treatment is especially indicated in purulent pleurisy.

SANFORD, Chicago.

A Case of Mediastinal Diaphragmatic Pleurisy. G. Cardelle, Bol. Soc. cubana de pediat. **2**:97 (Feb.) 1930.

A boy, aged 3, suffered for fifteen days from dyspnea and a fever of 39 C. The physical signs were negative, as were the results of a pleural puncture. A roentgenogram, however, showed a characteristic shadow. A similar case was found in a child, aged 2. The difficulty of diagnosis in this form of pleurisy is discussed. Litten's and Paillard's signs are not to be relied on. A pleural puncture may show nothing. A roentgenogram showing a band of dense matter at the inferior costophrenic angle is diagnostic.

Sanford, Chicago.

Large Cell Splenohepatomegaly. E. Stransky, Jahrb. f. Kinderh. **126**:204 (Jan.) 1930.

Three children in the same family died in early infancy of cachexia due to large cell splenohepatomegaly. In one case the diagnosis during life was Niemann-Pick's disease, but after autopsy, Gaucher's disease. The author gives his reasons for regarding the two diseases as identical.

Clausen, Rochester, N. Y.

Toxic Action of Viosterol in a Case of Aplasia of the Thyroid. N. M. Nikolaeff and J. W. Zimbler, Jahrb. f. Kinderh. **126**:222 (Jan.) 1930.

An infant was slow in growth and development, with subnormal temperature, constipation and slow pulse rate (80), but did not show marked signs of hypothyroidism until the eighth month. At 1 year of age, it was found to have 15 mg. of calcium and 2.8 mg. of inorganic phosphorus per hundred cubic centimeters of serum. No note is made as to the presence or absence of rickets. Viosterol, "3, 5, 6 and 10 drops," was given; the dose after the third week appears to have been 4 mg. a day. At first, improvement was noted; but after twenty-five days, vomiting and loss of weight occurred. The amount of calcium fell to 14.4, and that of phosphorus rose to 4. The child died of pneumonia, noma and septicemia. Autopsy showed complete absence of thyroid tissue; one parathyroid gland was found. Deposits of calcium were found in the walls of the small arteries of the kidneys, in the connective tissue around the lymph nodes and the suprarenal glands and in the medulla of the suprarenal glands. Necrosis was observed in the mucosa of the small intestine. The authors believe that probably the latter change and certainly the pathologic calcification were caused by viosterol.

Clausen, Rochester, N. Y.

Chylous Ascites in Childhood. S. Bruchsaler, Monatschr. f. Kinderh. **45**:439 (Dec.) 1929.

An infant, aged 4½ months, had sufficient swelling of the abdomen to interfere with its health and comfort. An exploratory puncture revealed a milky fluid full of fat globules and only a few lymphocytes. The results of chemical examination of the fluid are given in detail. This is the only report of such a case in an infant. An exploratory operation failed to reveal the cause. On postmortem examination no cause for the condition was found although there was a pea-sized edematous diverticulum in the cardia of the stomach, with some edema in the periesophageal tissues. Possibly this was concerned in the etiology. In none of the few cases reported has the anatomic cause been discovered.

Gerstley, Chicago.

Essential Hypertension in Early Childhood. Erich Holzmann, Monatschr. f. Kinderh. **45**:449 (Dec.) 1929.

A boy, aged 4½, complained of pain in his feet. At times he had pain in his ears but no discharge. The blood pressure was 140 systolic and 95 diastolic.

Some days after his admission, convulsions developed and the systolic pressure reached as high as 160. Lobar pneumonia intervened, during the course of which the pressure sank to 105 but returned again after recovery. There were no other observations and no changes in the heart or the urine. The cholesterol in the blood increased at times to 212 mg., and receded again to 120 mg.

There was nothing in the family history to give a clue. The child was discharged after a time and returned some months later in good condition, with the blood pressure down to 100.

GERSTLEY, Chicago.

MEDICAL OR SURGICAL TREATMENT FOR PYLORIC STENOSIS? W. BIRK, Monatschr. f. Kinderh. **45**:481 (Jan.) 1930.

If a child with pylorospasm, who is held on a maintenance diet of breast milk given in small doses, does not show marked improvement in four days, Birk orders a Rammstedt operation. A maintenance diet on breast milk is one tenth of the body weight; the normal diet is one sixth of the body weight. If vomiting ceases, the diet should gradually be increased. Should vomiting start again, following the increase, one must either go back to the maintenance diet or resort to surgery. In all cases the surgeon should be consulted while the child is still in good condition.

GERSTLEY, Chicago.

A CASE OF KALA-AZAR. B. OSTROWSKI, Monatschr. f. Kinderh. **46**:193 (March) 1930.

A boy, aged 8, suffered from malnutrition and exhibited a very large liver and spleen. All the usual tests gave negative results. There was a leukopenia of 3,400 and a continuous fever. Anemia developed, the red cells numbering 3,600,000 and the white cells 1,900; there was a tendency to lymphocytosis. A splenic puncture established the diagnosis and the child made a recovery under treatment with antimony. The author makes a point of the importance of the temperature curve. On many days two peaks are shown instead of the usual single peak of sepsis. This type of fever is characteristic of kala-azar.

The disease is readily confused with Banti's disease, though in the latter case leukopenia is not so marked.

GERSTLEY, Chicago.

NORMAL BLOOD PRESSURE FROM THREE TO TWENTY YEARS: A RESEARCH ON 1,932 CHILDREN AND YOUNG PEOPLE IN OSLO. A. SUNDAL, Ztschr. f. Kinderh. **47**:742, 1929.

The systolic blood pressure was measured with the Riva-Rocci-Recklinghausen mercury manometer with a band 12 cm. wide, in 1,932 children, 1,049 boys and 833 girls, from 3 to 20 years of age. The pressure was taken in the sitting position by the palpatory method and was studied in relation to age, size, weight, sex and social class. The blood pressure curve climbs with increasing age, though not regularly, and there is a proportionately sharp ascent in girls from 9 to 12 years of age, and in boys from 10 to 13 years; after the fifteenth year in girls (about 110) and after the seventeenth year in boys (about 115) there is no further increase. The relation between blood pressure and length and body weight is similar; with the increase of size and weight, the blood pressure climbs, and one remarks the proportionate quick climb in the size and weight groups which corresponds to the 9 to 12 year group in girls and the 10 to 13 year group in boys. For the same age, blood pressure in children in the high school is somewhat higher than in those in the grade school. This difference in relation to social station is explained by the different physical development. In children of the same age, blood pressure is a little higher in the taller and heavier.

EMERSON, Boston.

ON BRONCHIECTASIS; CIRRHOSIS AND BLEEDING OF THE LUNG, N. P. TENDELOO, Nederl. tijdschr. v. geneesk. **1**:3 (Jan. 4) 1930.

Bronchiectasis may be divided into two forms, (1) congenital and (2) acquired after birth. To the first form only malformations belong. The author discusses the second group especially. The form, number and extent of bronchiectatic cavities may be quite different. Nearly always the dilatations of the bronchi are found in the caudal parts of the lung. The author mentions the diseases that may give rise to bronchiectasis and discusses in detail the ways in which bronchiectasis is caused by these diseases. The significance of a higher intrabronchial air pressure during inspiration is denied. Cirrhosis of the lung often gives rise to the development of bronchiectasis, but the origin of this depends on several factors which he discusses. Some cases of bronchiectasis found in children are given as illustrations. The two important symptoms, clubbed fingers and hemoptysis, are described in detail.

The protection against bronchiectasis must be principally a protection against diseases and injurious factors that may give rise to peribronchitis and other proliferative inflammations. In this regard, whooping cough, measles and chronic influenza also deserve special attention.

VAN CREVELD, Amsterdam, Holland.

Nervous Diseases

THE RELATION OF MINOR NERVOUS DISTURBANCES TO TETANY IN CHILDREN. W. RAY SHANNON, Arch. Pediat. **46**:679 (Nov.) 1929.

The author presents a syndrome with the following manifestations: sleeplessness, night terrors, sleep-walking, emotional irritability with a tendency toward crying, fits of temper, apprehensiveness, head-rolling, bed-shaking, enuresis, anorexia and various other behavioristic manifestations, the predominating tendency being that of emotional irritability. He thinks that these symptoms are closely related to tetany and that they differ from frank tetany only in degree, in that they occur in persons who approach the tetanic state or who occupy a position somewhere between the normal and the tetanic state. Twenty-one cases are reported.

Infectious diseases and a constitutional strain appear to be precipitating factors. The underlying cause is not absolutely determined, but the weight of evidence suggests hypoparathyroid function and a disturbance of related unknown mechanisms as fundamentally at fault. The blood calcium is slightly below the commonly accepted normal; viz., from 9 to 11 mg. per hundred cubic centimeters. The Chvostek and Trousseau signs are often present. Therapy that has for its object a raising of the blood calcium is effective; hence the administration of parathormone, activated ergosterol and calcium in some form is indicated. The value of sunlight, cod liver oil and the ultraviolet ray is suggested.

WILSON, Norfolk, Va.

POSTVACCINAL ENCEPHALOMYELITIS. JULIAN GRAUBARTH, Arch. Pediat. **46**:703 (Nov.) 1929.

A girl, aged 5 years, was admitted to the hospital in an unconscious state. Subsequent events showed that she was suffering from acute encephalitis. She was vaccinated against smallpox one week prior to the onset of the disease. The reaction was only moderate, and with very little local evidence. Onset of the disease occurs from four to fifteen days after vaccination. About 50 per cent of patients recover.

WILSON, Norfolk, Va.

INTRACRANIAL HEMORRHAGE. DORRELL G. DICKERSON, Northwest Med. **28**: 535 (Dec.) 1929.

Extradural hemorrhage is usually the result of a violent cranial injury, but the skull need not be fractured, nor need there be visible signs exteriorly. There is usually a period of unconsciousness followed by a period of freedom from symptoms other than headache, after which there are signs of increasing intracranial pressure, drowsiness stupor, coma, slowing of pulse, rising blood pressure, edema and choking of the optic disks. The rapidity with which these phases follow each other depends on the size of the extradural vessel broken. This is usually on the lateral aspect of the cerebrum in the temporosphenoidal region. It is interesting to note that general body burns may cause this condition as well as the commonly accepted etiologic factors. The focal symptoms are twitching, motor aphasia, paresis of face or arm, signs of medullary compression. The spinal fluid may show blood if a tear of the dura is present.

Subdural hemorrhage is more frequent than extradural and is commonly found in fractures of the base. There may be a profuse hemorrhage with coma as the only symptom, or there may be lesser hemorrhages with drowsiness, convulsions, paralyses, the Babinski reflex and loss of deep reflexes. Exploration usually reveals small scattered hematomas at the base in the middle fossa, blood-tinged spinal fluid which is usually under moderately increased pressure.

Subarachnoid hemorrhages produce either a mild symptomless condition or profound bleeding with early death. Often there are only headache, mild mental symptoms and blood-tinged fluid.

Cortical hemorrhage may be diffuse over the brain or local; in the latter case, Jacksonian seizures may occur.

Intracerebral hemorrhage is most common in leakage from the left lenticulostriate artery in persons with atheromatous vessels, or in the late stages of syphilis. It also occurs in hemorrhage within cranial neoplasms, especially spongioblastomas.

Intraventricular hemorrhage occurs in arteriosclerosis, syphilis and tumor of the brain. It has a very rapid onset, with profound coma, altered cardiac and respiratory action, spasticity, cyanosis and free blood in the spinal fluid.

Chronic subdural hemorrhage is characterized by an injury with apparently complete recovery. There is a gradual accumulation of blood beneath the dura, which becomes encysted. The clot finally reaches such a size that compressive symptoms occur: headache, vomiting, lack of attention, mental dulness, memory defect, stupor, coma, convulsive phenomena and changes in the eyegrounds.

Intracranial hemorrhage of the new-born usually follows either a rapid or a prolonged delivery or occurs when there is hemorrhagic disease. The symptoms are obscure, mainly drowsiness and failure to nurse well. There may be convulsions, cyanosis, a tense fontanel, cervical and general rigidity, and bloody spinal fluid. Indications are for early drainage and an exploratory operation.

The general indications for operation in intracranial hemorrhage are increasing intracranial pressure, the absence of surgical shock and the appearance of focal neurologic symptoms.

SCOTT, Philadelphia.

THE EPIDEMIC OF DISSEMINATED INFLAMMATION OF THE NERVOUS SYSTEM IN POLAND IN 1928. EDWARD FLATAU, Encéphale **24**:619 (July-Aug.) 1929.

During 1928, the author observed cases which were impressive because of the singularity of the symptoms. The onset was sudden, sometimes with pains of peculiar localization or bizarre hyperesthesias, sometimes with pareses or paralyses. The symptoms included cranial nerve disturbances such as facial palsy; unilateral visual alterations (haziness and blurring); occasional involvement of the sphincter; cerebral symptoms of convulsion or speech disorder; a normal temperature or but slight elevation and then only for a short time, and usually little disturbance of sleep. All symptoms were mild and often fugacious; they did not necessitate confinement to bed. The total series comprised about twenty-five cases, of which seventeen are summarized in the paper; two fatalities occurred. These all con-

stituted cases of an epidemic of local proportions that were seen by the writer in his private and consulting practice. The majority of the patients were children between the ages of 11 and 13 or young adults; one patient, aged 67, is listed.

The histopathologic study in one case showed infiltration of the central ganglia, of the spinal cord, and about the roots of some of the peripheral nerves. A neurologic reaction was manifest, with a tendency to the accumulation of these cells about the vessels; neuronophagia was rarely observed. The meninges were the site of extensive infiltrations, especially about the pons.

Then follows a comprehensive review of the case studies in the literature of those conditions which fall into the three categories of endemic encephalitides per se, of encephalitides and myelo-encephalitides complicating acute infections and of so-called sclérose en plaque. Basing his statements on all these studies, the author has arrived at the conclusion that the appearance of small foci of epidemic or endemic diseases approximating a disseminated myelo-encephalitis is probably to be considered as having a relationship to the large epidemic of epidemic encephalitis. It is possible, with certain reservations, that one would be obliged to classify in the same group the nervous complications that are so frequently observed in recent years in the course of the infections of variola, varicella and rubeola. The augmentation of the number of acute and abortive cases of sclérose en plaque imposes also the hypothesis of the influence of the major epidemic. It is, however, impossible to solve as yet the question as to whether the resistance of the human organism was lowered under the action of the epidemic or whether the same virus was responsible for the pathologic condition in all these groups.

ANDERSON, Los Angeles.

TEN YEARS IN REFLEXOLOGY, 1917-1927. JOHANN SUSMANN GALANT, Monatschr. f. Kinderh. **45**:404 (Dec.) 1929.

The author gives the results of a ten years' study of the reflexes of infants. In 1917 he described an arching of the back that resulted from stroking the back of an infant as it lay on its stomach. The writer had originally planned to study the anatomy of the nervous system but although he was an able student his drawings were so poor that Professor Feer suggested that he take up the study of reflexes. His first contribution was the reflex described, which he interprets as of the same significance as the Babinski reflex. He has described a number of reflexes occurring in the small muscles of the hand caused by tapping the muscles of the thumb or the little finger. There is also the Galant biceps reflex. This appears to be nothing more than the usual biceps reflex, except that it is obtained by pinching the biceps between the thumb and first finger. The spino-iliac abdominal reflex also described by him is obtained by percussing the anterior-superior spine. This periosteal reflex is obtained in 89 per cent of cases. It is increased when the usual skin reflexes are diminished.

The writer then continues his discussion of reflexology along more philosophical lines and takes his reader through fields of vaginismus on one side and through a menagerie of snakes and decapitated beetles, until he leaves the simple-minded pediatrician far behind.

GERSTLEY, Chicago.

ETIOLOGIC FACTORS OF EPILEPSY IN CHILDREN. T. P. SIMPSON, Collected Papers, Psychiatric Clinic, First Moscow State University **3**:274, 1929.

The author studied 296 children who were referred to the clinic for convulsive disorders conducted by the Moscow Board of Health. Most of the children were under the age of 3. One hundred and twenty were found to be suffering from spasmophilia or allied conditions. The author differentiates spasmophilia from epilepsy and gives her diagnostic criteria. Spasmophilia manifests itself in asphyxia due to a laryngeal spasm or to other causes. It is bilateral and is usually not followed by loss of consciousness and sleep. The attacks usually come on during the day and have a relationship to some psychogenic factor such as fright, punish-

ment, etc. After the age of 2, spasmophilic attacks cease. The intellectual development of such children is normal. Epileptic seizures are observed in children of all ages; they come on very often without special cause. The seizures begin often during sleep, are at first unilateral, are accompanied by loss of consciousness and are followed by deep sleep. These attacks often leave some neurologic residuals, and parallel with this there is intellectual retardation of the child, with marked personality change and often a complete alteration of the psyche.

In describing the spasmophilic conditions, the author states that the attack either would stop during the tonic convulsion of the whole body or would go on to clonic convulsions with loss of consciousness and light reflex and involuntary micturition and defecation. Quite often the first attack occurred during the course of an infection with high fever; then it would recur under psychic stimuli and would thus appear to be functional in origin. Once equilibrium is disturbed, comparatively insignificant factors may give rise to a seizure. The personality of children with spasmophilia shows a tendency toward marked irritability, restlessness, aggressiveness and, at times, rather antisocial behavior.

One hundred and seventy-six children had rather definite epileptic seizures. The ages in this group varied from infancy to 14. Hereditary factors were present in more than half of the cases. In 104 of these cases one could trace a definite organic etiology; 4 children had an endocrine toxic epilepsy, and in 68 cases no etiologic factors could be ascertained. In the first group of 104 children, encephalographic studies were made by the lumbar route; in about half of these children some definite pathologic condition of the brain, such as residuals of encephalitis, trauma, cortical atrophy, etc., was observed. In a few cases, there were systemic intoxications such as uremia, enteritis and nephritis. In 5 cases, intestinal parasites were the only thing discovered which could account for the attack. The author calls attention to a large number of minor neurologic signs found in these children.

The aura consisted often of visual hallucinations. The personality change consisted in the appearance of either sadistic or masochistic trends, with the development of what Jones has described as homosexual character traits such as meticulousness, accuracy, stinginess, etc. While the adult epileptic patient is usually sluggish and somewhat ponderous, the epileptic child is very restless, noisy and somewhat hypomanic. In epileptic children one observes tremendous resentment toward authority, with severe outbursts of temper when crossed.

In the cases of nineteen children, intra-uterine infections and toxins played an important rôle. There was either syphilis or alcoholism of one or both parents. The author calls these cases constitutional epilepsy. In these cases the attacks developed soon after birth and the children were extremely difficult to handle on account of severe temper tantrums. The author calls these children congenital psychopathic patients.

The author comes to the conclusion that encephalography is an extremely important aid in studying epilepsy in children. It often reveals marked pathologic changes of the brain, even when a neurologic examination gives absolutely negative results. The etiology of epilepsy is extremely complex, but given a constitutional predisposition to convulsive manifestations, slight toxic factors may elicit the seizures. A thorough study of all factors involved, metabolic, psychic and neurologic, will help to narrow down the extremely large groups of the idiopathic epilepsies.

KASANIN, Boston.

Diseases of the Eye

OCULAR LESIONS IN FETAL SYPHILIS. JONAS S. FRIEDENWALD, Bull. Johns Hopkins Hosp. **46**:185 (Feb.) 1930.

The literature is discussed and the author notes the scanty pathologic and clinical information on ocular lesions in fetal syphilis. The complete autopsy observations in nine cases are described. A clinical classification of the ophthalmoscopic pictures is given on the basis of this pathologic analysis.

1. Circumscribed chorioretinitis. These cases show focal lesions, sometimes multiple, in the choroid and retina. They occur at any time in the life of a person with congenital syphilis, antenatal, or postnatal, and are not essentially different from similar lesions in acquired syphilis, or in nonsyphilitic ocular disease. The active stages have not heretofore been observed either clinically or pathologically in the fetus or the infant. They produce dense, circumscribed scars which reveal themselves ophthalmoscopically as chalky white patches surrounded by heaped-up choroidal pigment.

2. Salt and pepper fundus. This ophthalmoscopic picture is characteristic of congenital syphilis, and since it is often found early in life the presumptive evidence is strong that it is the outcome of fetal or early infantile inflammation. It represents the end-result of a lesion, the active stage of which is unknown to the ophthalmoscopist. The early stages of this lesion are characterized by a diffuse infiltration of the choroid with inflammatory cells, the reaction being most intense in the superficial layers of the choroid, namely, the choriocapillaris. Subsequently, a fine diffuse scarring develops, with great disorganization of the choroidal capillary bed. Finally, the layer of pigment epithelium and the rods and cones, which are little affected by the inflammatory process but which depend on this capillary bed for their nutrition, become atrophied and disorganized, the pigment being heaped up at one point and absent at the next. The resulting peppery appearance of the fundus is easily understood.

3. Retinal scarring with atresia of the retinal blood vessels and optic atrophy. This somewhat more rare ophthalmoscopic picture is generally associated with lesions of type 2, and is also to be attributed to an inflammatory process, the active stage of which has occurred early in life. It is characterized by the formation of widespread veils of connective tissue in the retina, together with marked atresia of the retinal blood vessels, with a muddy white appearance of the disk, and a blurring of its margins.

4. Retinitis pigmentosa. Under this descriptive name are grouped together a medley of cases of widely divergent pathogenesis. The relatively common familial type of this disease has, of course, nothing to do with syphilis. The same may be said of those extremely rare cases which develop after severe septic infections. The syphilitic cases of retinitis pigmentosa are separable into two groups: (1) those which develop in infancy and which are merely an exaggeration of the "salt and pepper" process, and (2) those which develop late in life. The latter cases are perhaps to be related to late syphilis of the central nervous system with which they are not infrequently associated.

LYTTLE, New York.

Diseases of the Ear, Nose and Throat

ACCESSORY SINUS DISEASE IN CHILDREN. I. R. VAILE, Canad. M. A. J. **22**:198 (Feb.) 1930.

The author cites his experience in the treatment of children for accessory sinus disease. The condition is frequently associated with diseased tonsils and adenoids but may exist independently or may even be made worse by their removal.

Eighty per cent of patients are cured by conservative measures. These consist of the use of a brand of mild silver protein after proper cleansing by suction methods and the use of radiant heat. Occasionally a radical operation is required. The importance of complete adenoidectomy is emphasized.

MOORE, Omaha.

THE ETIOLOGY OF A CASE OF LATENT OTITIS MEDIA WITH SECONDARY DYSPEPSIA AND ACIDOSIS. SALVADOR E. BURGHI, Arch. Españ. de pediat. **13**:705 (Dec.) 1929.

A poorly nourished infant, aged 17 months, showed evidence of rickets.

Following an attack of rhinopharyngitis a latent otitis media developed with secondary dyspepsia, marked dehydration and intoxication.

Free paracentesis of both ears and administration of fluid caused the disappearance of all toxic phenomena within forty-eight hours and complete restoration to health. Excessive heat was not a factor in the development of the symptoms.

SCHLUTZ, Minneapolis.

TOPOGRAPHY AND MECHANISM OF THE TONSILS. B. CHORONSHITZKY, Monatschr. f. Ohrenh. **63**:1058 (Oct.) 1929.

On the basis of his personal studies and a review of the literature, Choronshitzky comes to the following conclusions: The anlage of the tonsils is developed in the interarcual tonsillar fossa under increasing positive pressure; thus, concentric layers of the peritonsillar connective tissue result, which form the basis of the capsule in the deep-seated tonsil. The pedicled tonsil, however, has no capsule. The last type of tonsil, therefore, cannot harbor a subcapsular abscess, and expulsion of its contents is far more easy than in the deep-seated tonsil. The double lobe of the tonsil is due to persistence of the embryonic intratonsillar fold, as von Hammar stated. The capsule caps the outer and upper surface of the tonsil, enclosing the fossa supratonsillaris. The fringe of the tonsil lies between the mucous membranes of the side wall of the pharynx and the interarcual fossa. It is due to this cap that the enucleated tonsil appears on frontal section shaped like an arabic six (6). On its dorsal surface, the subcapsular abscess forms protuberances of varied size. Evacuation of chronic subcapsular abscesses are of far-reaching importance in various diseases of the tonsils. However, opening of a peritonsillar abscess with a stump hook by way of the lacuna is dangerous, and the result is doubtful. Recurrences after tonsillectomy are prevented only if the entire tonsillar fossa is enucleated.

[ARCH. OTOLARYNG.]

Diseases of the Skin

A NOTE ON COMBINED CONGENITAL ECTODERMAL DEFECTS. F. PARKES WEBER, Brit. J. Child. Dis. **26**:270 (Oct.-Dec.) 1929.

The author briefly mentions congenital ectodermal defects of the teeth, the hair of the head and the nails.

LANGMANN, New York.

INFANTILE ACRODYNIA. MARIO ARTOM, Gior. ital. di dermat. e sifil. **70**:810 (Aug.) 1929.

The author reviews the history of this disease, comparing the epidemic condition in adults and the newly described infantile form of the disease. He reports three cases observed by him in Novara, Italy, and describes in detail the psychic, neuromuscular, cutaneous and mucous symptoms. He deals at length with the question of differential diagnosis of arsenical poisoning, pellagra and ergotism.

From his studies and observations, the author concludes that acrodynia is due to a diffuse involvement of the neuro-axis and of the vegetative system produced by a virus still unknown but probably similar to the germ of epidemic encephalitis and of poliomyelitis, i. e., a neurotropic virus.

PARDO-CASTELLO, Havana, Cuba.

ECZEMA FOLLOWING VACCINATION. E. RULLMANN, Arch. f. Kinderh. **88**:20 (July 12) 1929.

Two cases are described. The first child was 1 year of age, and the lesions developed in seven days; the eruption was generalized over the arms, legs and face. In the second child, 11 years of age, the lesions also developed in seven days. Treatment was of no avail.

SANFORD, Chicago.

PASSIVE CONGESTION OF THE SKIN IN CHILDHOOD. H. SECKEL, Monatschr. f. Kinderh. **45**:394 (Dec.) 1929.

The writer believes that the clubbed fingers and toes occurring in chronic circulatory conditions are simply noticeable changes accompanying general changes of the entire integument.

He submits a table indicating changes in the skin in a variety of different respiratory diseases, chiefly pneumonias and empyemas. In many of these there was a pasty condition of the skin verging on edema. Telangiectases appeared and in proximity to them hypertrichosis developed. The favorite location of the latter was on the back between the shoulder blades, also on the extensor side of the upper arm and thigh.

The explanation for these areas of passive congestion in the skin is not clear, but they may be due to a toxic effect on the capillaries.

GERSTLEY, Chicago.

Surgery and Orthopedics

CONGENITAL ABSENCE OF CRUCIAL LIGAMENTS: RESULT AFTER FASCIAL GRAFT. H. A. T. FAIRBANK, Proc. Roy. Soc. Med. **23**:257 (Jan.) 1930.

A patient was first seen in 1924 on account of congenital subluxation of the right knee. There was some genu valgum. The fibula was diminutive, with marked valgus of the foot, dislocation of the peroneal tendons, absence of the outer part of the foot and of two toes, and adduction of the foot. Midtarsal and subastragaloid arthrodesis with correction of the valgus was performed. The knee was fixed in plaster in flexion for two years without result. In 1927 the knee-joint was opened, and as the crucial ligaments were completely absent an Alwyn-Smith operation was performed. The report is accompanied by roentgenograms showing the bones and the result of the operation.

WILLIAMSON, New Orleans.

TREATMENT FOR PLEURAL EMPYEMA WITH A NEW CHEMOTHERAPEUTIC PREPARATION. U. FRIEDEMANN, München. med. Wchnschr. **76**:1954 (Nov. 22) 1929.

Friedemann discusses primarily the treatment for postscarlatinal empyema. In his experience, the only form of treatment which formerly resulted in cure was surgical intervention. However, he has treated four patients successfully by aspiration and injection of a new dye, acridine. In four other patients treated with acridine an operation was necessary. The dye loses its bactericidal effect in the presence of thick pus, so treatment must be started early. Subcutaneous extravasations of the dye may cause necrosis. The author warns against injection into the parenchyma of the lung. Although the successful results are few, the author feels that in view of the unsatisfactory results in the past, the new dye has promising possibilities.

BRAHDY, Mt. Vernon, N. Y.

NONSURGICAL REDUCTION OF SUPRACONDYLAR FRACTURE OF THE HUMERUS IN CHILDREN. A. BECK, München. med. Wchnschr. **76**:2161 (Dec. 27) 1929.

One of the most frequent fractures during childhood is the supracondylar fracture of the humerus. Beck describes a nonsurgical reduction which he employed successfully in four children, three of whom also had a dislocation of the elbow. The reduction is performed under deep anesthesia. Fixation of the parts with flexion at the elbow is maintained by a plaster of paris splint applied directly on the skin. The hand is not covered, and in order to prevent contractures the author stresses frequent movements of the fingers and wrist. The splint is kept on for four or five weeks.

BRAHDY, Mount Vernon, N. Y.

Miscellaneous

THE THERAPEUTIC VALUE OF RADIATION. ETHEL M. LUCE CLAUSEN, Medicine **8**:419 (Dec.) 1929.

Radium and roentgen therapy are not considered. After a brief historical sketch, there is a statement of general criticism of the papers that have been written on clinical radiation. Its uncontrolled use is condemned entirely. The author states that in rickets only is radiation known to have specific action, and that in very few diseases, possibly only in lupus vulgaris and tuberculosis of the bones and glands, are clinical results good enough to warrant radiation as the treatment of choice. Such studies as those of MacKay's should do something to stem the tide of popular enthusiasm.

The apparent cure of certain skin diseases, "after all other methods have failed," does not properly show the effect of the former treatment. In many treatises on radiation, not even the source of light has been mentioned, to say nothing of the voltage, amperage, etc. The usual method of dosage is entirely empiric; the erythema dose is only a rough index of the tolerance of the patient to ultraviolet rays. At present, the whole knowledge of light therapy is indefinite.

The experiments on the cure of rickets and those leading to the discovery of viosterol are reviewed. The toxic effects of overdosage with viosterol are apparently most important because of an excessive deposition of calcium in various body tissues. This is brought about by overdosage, but the possibility of culminative action from repeated smaller doses should be investigated.

The author discusses Rollier's work on tuberculosis. It is to be noted that when pigmentation occurs, the healing of tuberculosis of the bones is hastened. Pigmentation is a protective spectrum; hence, an explanation of its action is less clear than it was before. The other factors of Rollier's treatment as well as the heliotherapy must be considered. Mayer reports excellent results in children from heliotherapy in the treatment for bone, joint, skin, and peritoneal tuberculosis, and a palliative effect in intestinal tuberculosis. In tuberculous adenitis better results are obtained with roentgen rays than with heliotherapy. In surgical tuberculosis, treatment with artificial light is disappointing. Sunlight is of doubtful benefit in pulmonary tuberculosis.

LoGrasso and Balberry, on the other hand, report favorable results with the use of heliotherapy in pulmonary tuberculosis, and state that the reason others have had unfavorable results is that the treatment has been haphazard. A gradual exposure of the whole body to sunlight, reaching a maximum of three hours a day, is best. In the height of summer the patients were exposed only in the early morning and in the late afternoon.

Finsen's workers, using his methods, have had good results in lupus vulgaris. Other workers, however, have not had as good results; some observers, however, using Finsen's methods have reported favorable results. With other skin diseases results have varied, and are altogether inconstant. The reports of results in idiopathic purpura hemorrhagica can hardly be depended on, since it is known that this symptom complex is subject to remission and variations of intensity.

It must be borne in mind that all exposures to light may be followed by serious pathologic conditions. Opinions on the development of pigmentation as a guide to benefits vary and are often diametrically opposite.

The effect of light from the mercury vapor quartz lamp as observed by MacKay is entirely negative. This whole phase of the subject is in a state of uncertainty, and at present the evidence is largely negative.

A caution is added that the public be protected against the indiscriminate use of "ultraviolet" lamps.

ROYSTER, University, Va.

THE RELATION OF BLOOD TRANSFUSION TO THE DISTURBANCE OF BLOOD CLOT FORMATION. R. A. KORDENAT, Mil. Surgeon **66**:206 (Feb.) 1930.

Clinically, in this series of cases, as much as 750 cc. of whole blood did not elevate the blood pressure to more than 15 mm. of mercury; it stopped bleeding

in each instance. There was no clinical evidence that blood transfusion disturbed blood clot formation, but, on the contrary, blood clot formation was undoubtedly aided by transfusion. Experimentally, an increase of the intra-arterial pressure from 80 to 100 mm. of mercury did not mechanically disturb a blood clot in a small artery.

SANFORD, Chicago.

THE PROPER CLOTHING AND SHOES FOR THE GROWING CHILD. ARTHUR H. GRAY, Northwest Med. **28**:324 (July) 1929.

1. Cotton is better than wool next the skin, as it is absorbent and less irritating.

2. Indoor clothing should be light when the home is maintained near 70 F.

3. Overdressing causes undue perspiration.

4. Clothing should be simple, light and loose.

5. In cold weather, the whole body, from the neck down, should be equally clad.

6. No tight-fitting or constricting articles, such as elastic garters, should be permitted.

7. The "bird's-eye" cotton diaper is the most porous and absorbent, and therefore the most suitable.

8. The diaper should be applied the "square" way.

9. Cotton or silk and wool shirts, opening in the front, should be used.

10. A sleeveless petticoat coming to from 6 to 10 inches below the feet should be worn, except in hot weather.

11. Stockings should be worn only in the daytime, and should be of cotton, silk or silk and wool.

12. Stockinette is the best material for a night gown.

13. The first shoes should be high, should have no heels and should conform to the shape of the feet. In winter the soles should be fairly thick.

SCOTT, Philadelphia.

METHOD FOR DETERMINING ON THE INFANT CADAVER THE DEGREE OF INTOXICATION OF THE NURSE. DERVIEUX, SZUMLANSKI and H. DESOILLE, Ann. de méd. lég. **9**:501, 1929.

Alcohol taken by a nursing woman can be detected in the milk within fifteen minutes of its ingestion, reaches a maximum after about forty-five minutes and can still be detected after four hours. The alcohol content of the milk in the stomach of the infant cannot be higher, but can be considerably lower than that of the milk when ingested. The alcohol content cannot be increased by fermentation of the sugar contained in the milk.

KUGELMASS, New York.

REPORT OF SIXTH FRENCH PEDIATRIC CONGRESS HELD AT PARIS, Sept. 30-Oct. 2, 1929. F. SAINT GIRONS, Nourrisson **17**:359 (Nov.) 1929.

1. Postoperative Pallor-Hyperpyrexia Syndrome of Ombrédanne: This syndrome was described by Ombrédanne in 1922. It occurs most often in infants under the age of 6 months, though occasionally in children up to 5 years of age. Many of these infants have been victims of hydrocephalus or of some congenital anomaly. The clinical picture is dramatic; the infant may develop marked pallor during the operation, followed in from six to ten hours by an abrupt rise in temperature to 40 C. (104 F.) and over. The fever is followed by severe pallor and profound prostration, at times interrupted by convulsions. Death supervenes in from twelve to sixteen hours after the operation. Recovery is exceptional. The syndrome has been reported as occurring much more frequently after opera-

tions around the face (mastoidectomy, plastic operations for harelip, removal of angiomas), but also has been reported in association with operations for hernia, intussusception and sarcoma of the kidney.

Despite numerous researches on the urine, blood, feces, cerebrospinal fluid and chemistry of the blood, the pathogenesis remains obscure. Some operators have held the anesthetic responsible, but this has been controverted by others. Hemorrhage, subacute septicemia, the thymus, suprarenal insufficiency, disorders of the liver, kidneys and heart, encephalitis and anaphylactic shock have all been under suspicion. Finally, the bulbar theory has received considerable favor. This is based on the premise that the bulbar thermoregulatory and vasomotor centers in the young infant are unstable and can be overstimulated by noxious afferent stimuli from the site of operation, resulting in hyperpyrexia and marked peripheral vasoconstriction. Rocher and Pecher are champions of this hypothesis.

The treatment prophylactically calls for omission of preoperative starvation, enemas and purgation, the administration of digitaline amorphe, the avoidance of loss of external heat by adequate swathing and the employment of a complete general anesthetic to prevent the transmission of nocent stimuli from the operative field to the bulbar centers. The operation should be conducted with the utmost dispatch consistent with good surgery. Postoperatively one resorts to infusions, injections of epinephrine and camphor in oil. With the advent of pyrexia, cold enemas are given and cardiac stimulation applied.

2. Sudden Death in Infants: This paper was read by P. Nobécourt and G. Boulanger-Pilet. They classify sudden deaths in infants as follows: 1. Sudden death may be due to failure or malfunction of some particular organ. There may be a sudden circulatory failure, a latent bronchopneumonia, some kidney dysfunction or disease of the digestive tract; e. g., a retropharyngeal abscess, a disorder of the central nervous system (meningeal hemorrhages) or some endocrinopathy. 2. Sudden death may occur during the course of an acute infection; for example, in typhoid fever which often escapes recognition in infants, diphtheria especially the atypical forms, occasionally in scarlet fever and whooping cough and the sudden death that frequently occurs in congenital syphilis. 3. Sudden death may occur in infants afflicted with eczema. These infants frequently die after only a few hours in the hospital. An explanation for these cases is that death is due to anaphylactic shock induced by breathing the germ-laden dust of the hospital wards. 4. Sudden death dependent on a hypertrophied thymus may occur when the thymus has encroached on neighboring organs (trachea, heart, blood vessels, nerves) or without evidence of pressure insult. Reference is made to the frequent concurrence of thymic enlargement and lymphadenopathy, also to the so-called status thymolymphaticus or the association of an enlarged thymus with vagotonia. E. Apert takes issue with these hypotheses denying the possibility of a purely thymic death. For him the pathologic thymus of infants is the small thymus and he directs attention to the fact that a normal thymus is subject to rapid fluctuations in size depending on its vascularity. He suggests the name "accordion organ." An enlarged shadow on the roentgenogram does not justify the diagnosis of enlarged thymus. 5. The sudden death of infants with spasmophilia can most often be assigned to a spasm of the glottis, though some cases may depend on cardiac failure. 6. Finally there remains an unclassified group which have been assembled under the sobriquet "sudden death diathesis."

3. Icterus of the New-Born: This paper was read by C. Rocaz, who reviewed the subject and reported on researches conducted by himself and his interns, Mme. Berchon and Mlle. Fiot. For many years it has been known that newborn infants possessed cholemia. In a series of fifty new-born infants, Mme. Berchon showed that this cholemia reaches its maximum on the third or fourth day and progressively recedes until its disappearance about the fourteenth day. During this same period a hemolysin has also been demonstrated. Mlle. Fiot

has shown that the red blood cells are more fragile at this age. However she was not able to show that the intensity of the icterus paralleled the degree of fragility.

At present there are two theories regarding the pathogenesis of icterus neonatorum: The first considers it as an hemolytic icterus due to the destruction of the excessive red blood cells present in the infant at birth, and the second theory postulates an insufficiency of the liver. P. Lereboullet invokes both factors. He believes that the fetus before term has cholemia. Before birth this excess of bile is disposed of through the placental circulation. After birth the tying of the cord cuts off this way of escape and the bile accumulates.

The presence of increased amount of hemolysin in the new-born serves to augment the cholemia. The excretory function of the liver not yet having been sufficiently developed to accommodate the abnormal amount of bile in the infant, this bile gains access to the circulation and diffuses through all the tissues, giving rise to the so-called idiopathic or physiologic type of icterus.

Sloboziano and Hersocovice recommended cincophen in the treatment for icterus neonatorum.

E. Lesne, A. Heraus and R. Waitz reported on a case in which there was complete absence of the bile duct and an atrophic gallbladder. The infant lived for two months and then died from a pulmonary infection.

J. Huber emphasizes the importance of congenital syphilis in the etiology of the congenital type of hemolytic icterus.

P. Lereboullet and his associates found cholemia in all of the seventeen new-born infants studied but only rarely did they find bile or urobilin in the urine. Polycythemia was observed in ten infants at the beginning of the icterus, but it did not persist. The fragility of the red cells was also found to be increased.

4. Edemas of the New-Born: The discussion was opened by J. Cathala who emphasized the point that these edemas are more likely to be due to metabolic disturbances than to disorders of the kidneys or the heart as in the adult. The true congenital type of edema is rare. The acquired edema may be either local or general. The local edemas are usually of slight import whereas the general edemas are often associated (1) with states of denutrition, (2) with certain diatheses, e. g., eczema or spasmophilia, and (3) with prolonged digestive disorders. The point is brought out that the water content of the new-born is higher than that of the adult (69:63 per cent). One must never lose sight of the possible syphilitic rôle in the edemas of infancy.

L. Ribadeau-Dumas emphasized the relative frequency of the benign type of edema in the new-born. He also remarked on the importance of congenital syphilis as an etiologic factor.

Lereboullet and Lelong also reported a case of edema due to syphilis. It was characterized by great edema and marked albuminuria. The blood cholesterol amounted to 290 mg. per hundred cubic centimeters. Under intensive antisyphilitic therapy recovery took place.

Lemaire and Debrousse reported on two cases of syphilis with anasarca. In the first case, a breast-fed infant showed no albuminuria and recovered with appropriate treatment.

Rohmer remarked on the transformation that takes place in infants at the age of about 5 months. He thought, therefore, that the edemas of the younger period should be differentiated from those of later infancy.

Halle observed two cases of anasarca associated with influenza and he believed this to be an etiologic factor in some cases.

McCLELLAND, Cleveland.

DISEASES OF CHILDREN IN 1929. P. LEREBOULLET and F. ST. GIRONS, Paris méd. **19**:381 (Nov. 2) 1929.

The year in France was marked from the standpoint of social hygiene by the establishment of many new organizations for infant welfare and prenatal care.

In the new-born the study of idiopathic icterus has been the prominent feature. Rosenbaum, Bertrand and Lereboullet have contributed to the study of the bile pigments in the blood of these children. The edemas of the new-born and of infants have been more carefully studied during the year due to the impetus given by Cathala who said that many cases were the result of metabolic disturbances. In infant feeding the tendency has been toward beginning solid foods earlier and toward the elimination of milk. This was first advocated in Germany, but has been carried on by Marfan. In rickets great strides have been made in the development of irradiated products for treatment. In the chronic infections, further study has been made showing the efficacy of B.C.G. vaccine in tuberculosis and syphilis, and its possible value in congenital heart disease. In the acute infections, noteworthy contributions have been the study of bronchopneumonia by Heraux, and Marfan's study of diphtheria.

SANFORD, Chicago.

CHANGES IN METABOLISM FOLLOWING THE USE OF PHENYLETHYLHYDANTOIN. OTTO BECK, Monatschr. f. Kinderh. **45**:486 (Jan.) 1930.

Phenylethylhydantoin has been used successfully in the treatment for chorea. However, when given for a time, fever develops. Beck studied the metabolism during this febrile period and found an increased excretion of nitrogen in the urine, an increase in ammonia nitrogen and a change of hydrogen ion concentration, first toward a prefebrile alkalosis and later toward a febrile acidosis. In this respect, this fever is identical with infectious fever.

Following this condition if another course of phenylethylhydantoin is given, one again gets an immediate febrile reaction with an exanthem and changes in the intermediary metabolism. The drug apparently produces hypersensitiveness.

GERSTLEY, Chicago.

THE TREATMENT FOR NUTRITIONAL AND INFECTIOUS DISTURBANCES WITH INJECTIONS OF HUMAN BLOOD. WALTER BAUMANN, Monatschr. f. Kinderh. **45**:509 (Jan.) 1930.

Having read the enthusiastic reports of many American writers on the use of injections of human blood, the writer tried this treatment in a number of conditions. He cannot confirm the American reports as to the value of this therapy in acute nutritional disturbances. Neither intramuscular nor intrasinus injections were of value.

In chronic disturbance, such as intestinal infantilism, at times he thought the treatment helped. In pneumonias, cases of sepsis, valvular infections of the heart and severe cases of scarlet fever he thought that frequent injections of 10 cc. were beneficial.

GERSTLEY, Chicago.

EXPERIENCES IN CHILD WELFARE. ARTHUR KELLER, Monatschr. f. Kinderh. **45**:523 (Jan.) 1930.

This was a lecture given before the congress of Berlin school doctors. Keller gives credit to Herman Cohn, an oculist, for being one of the first in the early nineties to recognize the importance of school hygiene and to emphasize the necessity for examinations of the eye. Keller then quotes a number of authorities as to the definition of the duties of a school physician. They agree that there can be no rigid rule, as much depends on the type and the location of the school and the intelligence of the teachers.

Keller has high ideals as to the duties of the school physician and as to the type of man who should accept such a position. He believes that the responsibility is grave and that the physician must take a personal interest in every child in the school. No matter what type of social activity and no matter in what country, every one of these welfare procedures is worth only as much as the person who conducts it.

GERSTLEY, Chicago.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Regular Meeting, Dec. 12, 1929

F. Elmer Johnson, M.D., *Presiding*

Blood Volume Studies in Dehydration. Dr. Rustin McIntosh.

Patients with dehydration, manifested by changes in the elasticity of the skin, a depressed fontanel, sunken eyes, etc., were subjected to study immediately on admission and before parenteral fluids had been given. The blood volume was determined by the carbon monoxide method, the plasma-cell ratio by the hematocrit, and the serum total base, chloride, plus bicarbonate by the usual analytic methods. In many cases the serum protein was also determined, sometimes with the refractometer, but in most instances by the Kjeldahl method with subtraction of the nonprotein nitrogen. Calculations from these data gave figures for total circulating plasma and for total plasma electrolytes. At the end of a period of from seven to twenty-three days, depending on the clinical course, the same procedures were repeated to determine values somewhere near normal for each patient. The treatment during the interval between determinations was symptomatic, and varied in individual cases; some patients received transfusions, others were given dextrose solution intravenously or subcutaneously and all received normal physiologic solution of sodium chloride parenterally, either intraperitoneally or subcutaneously. Neither bicarbonate nor lactate was used.

The behavior of individuals varied greatly, so that it was not possible to draw general conclusions regarding the changes occurring in dehydration. Five slides were shown, depicting the course in five separate cases. One or more examples of the following phenomena were demonstrated:

There was a lowering of total blood volume in dehydration, with the essential change occurring in the plasma fraction, the cell volume remaining constant.

A lowering of serum electrolyte concentration occurred, involving mainly the total base and chloride components. Usually, though not invariably, the bicarbonate concentration also decreased in dehydration. The undetermined anion component, representing lactate, sulphate, phosphates and other acid radicles, often showed an increase, although this was not uniform.

Depression of plasma volume occurred occasionally without depression of bicarbonate concentration.

The loss of total plasma electrolyte was more marked than the lowering of serum electrolyte concentration when both were measured as percentage deviation from the presumably normal value found. Therefore, in clinical dehydration, the question may be raised whether the loss of electrolyte is not the primary disturbance, to which the loss of water is secondary. If this should be found to be true, the term "dehydration" would offer a one-sided description of the facts.

Severe acidosis (30.5 volumes per hundred cubic centimeters of carbon dioxide combining power) could be cured by the parenteral administration of normal physiologic solution of sodium chloride alone, without the use of bicarbonate or lactate either parenterally or by mouth.

The behavior of the plasma protein component was not uniform: Sometimes dehydration was accompanied by a decrease in the total plasma protein, suggesting that the fluid leaving the circulation under these conditions contains protein in addition to electrolytes and may possibly approach the composition of normal plasma, as pointed out by Darrow and Buckman; at other times, there was a

decrease in total plasma protein during convalescence from dehydration, a possible explanation for which is the starvation to which these patients were subjected in the course of their treatment.

DISCUSSION

DR. OSCAR M. SCHLOSS: By means of blood volume determinations Dr. McIntosh has thrown new light on the blood changes that occur in dehydration. He has rendered it possible to consider these changes in a quantitative way rather than in the purely qualitative fashion hitherto employed. His statement that the loss of electrolytes may be a primary factor in dehydration is interesting. It seems very probable that what is actually lost from the organism is not water containing varying amounts of electrolytes but tissue and plasma water containing in solution definite concentration of salts. This view was advanced some years ago by Gamble who has cited much evidence in its support.

In my opinion the administration of bicarbonate is unnecessary in most cases of acidosis which occur in dehydration. By means of subcutaneous injections of large amounts of normal physiologic sodium chloride or Ringer's solution in connection with the intravenous administration of dextrose solutions, severe acidosis can be corrected. Even though the plasma bicarbonate is below 20, complete restitution of the blood bicarbonate can be effected by the means described. It is, of course, possible that bicarbonate may be of use in selected cases in which the continued loss of base has caused marked lowering of the total base of the organism, but I am convinced that it is unnecessary in the average case. I am certain that large amounts of bicarbonate, especially by intravenous injection, may do great harm.

I feel that one should be a little cautious in drawing conclusions from determinations of plasma protein. In the first place, little is known of its formation or destruction. Of importance is the fact that unless one knows the concentration of plasma protein before dehydration occurs it is difficult to draw conclusions from its determination in the presence of dehydration. For example, plasma protein of 6 per cent in a dehydrated infant who was previously marasmic may actually represent an increase although this figure may be normal for a well nourished infant of the same age.

THE MINERAL METABOLISM IN DIARRHEA. DR. L. EMMETT HOLT, JR.

The data presented were obtained from unpublished observations of Holt, Courtney and Fales at the Babies' Hospital, New York City. The mineral metabolism was studied by means of experiments on the balance of normal infants and of those with mild and severe diarrhea. The following tables, in which the metabolism is calculated for a period of twenty-four hours, represent averages of (1) twenty-one observations on normal infants, (2) twenty observations on infants with mild diarrhea (untreated) and (3) five observations on infants with severe diarrhea (untreated).

TABLE 1.—*Metabolism of Normal Infants*

	Sodium	Potassium	Calcium	Magnesium	Chlorine	Phosphorus*	Base	Acid
Intake, Gm.	0.355	1.136	1.272	0.126	0.731	0.953	....	....
Urine, Gm.	0.239	0.604	0.023	0.016	0.523	0.350	....	....
Stool, Gm.	0.025	0.187	0.903	0.081	0.032	0.365	....	....
Retention, Gm.	0.091	0.345	0.394	0.029	0.176	0.238	....	....
Retention, milli-equivalents	3.9	8.8	17.3	2.4	4.9	21.1	32.4	26.0
Intake retained, per cent	25.6	30.4	31.0	23.0	24.1	25.0	....	....
Excretion in urine, per cent	90.5	76.4	2.3	16.5	94.2	49.0	....	....

* The valence of phosphorus is taken as 2.75 in all these experiments, this figure being based on the quantity of phosphorus in bone and in other tissues at this age. The assumption was made that phosphorus in bone had a valence of 3, and that phosphorus in the tissues had a valence of 1.8.

TABLE 2.—*Metabolism of Infants with Mild Diarrhea*

	Sodium	Potassium	Calcium	Magnesium	Chlorine	Phosphorus	Base	Acid
Intake, Gm.	0.281	0.816	0.729	0.083	0.538	0.540	....	....
Urine, Gm.	0.123	0.256	0.015	0.010	0.242	0.187	....	....
Stool, Gm.	0.134	0.303	0.530	0.052	0.135	0.214	....	....
Retention, Gm.	0.024	0.257	0.184	0.021	0.161	0.139	....	....
Retention, milli-equivalents	1.0	6.6	9.2	1.7	4.5	12.3	19.0	16.8
Intake retained, per cent	8.5	31.5	25.2	25.3	29.9	25.7	....	....
Excretion in urine, per cent	27.9	25.8	2.8	16.1	64.2	42.6	....	....

TABLE 3.—*Metabolism of Infants with Severe Diarrhea*

	Sodium	Potassium	Calcium	Magnesium	Chlorine	Phosphorus	Base	Acid
Intake, Gm.	0.261	0.519	0.665	0.060	0.441	0.454	....	....
Urine, Gm.	0.024	0.166	0.008	0.004	0.102	0.125	....	....
Stool, Gm.	0.474	0.543	0.643	0.078	0.354	0.344	....	....
Retention, Gm.	0.237	0.190	0.014	0.022	0.015	0.015	....	....
Retention, Milli-equivalents	10.4	4.9	0.7	1.8	0.4	1.3	16.4	1.7
Intake retained, per cent	90.8	36.6	2.1	36.7	3.4	3.3	....	....
Excretion in urine, per cent	4.8	23.4	1.2	4.9	22.4	26.7	....	....

The figures indicate that diarrhea is accompanied by an inadequate mineral retention, negative mineral balances being found in the more severe cases. Cases of mild diarrhea show a failure to retain fixed base as compared with fixed acid, and cases of severe diarrheas a far greater loss of fixed base than of fixed acid from the body. Excessive loss of fixed base as compared with fixed acid seems sufficient to account for the majority of instances in which acidosis develops during diarrhea. The loss of fixed base takes place largely through the intestines, and may be attributed to loss of the alkaline digestive secretions, as suggested by the experiments of Gamble on animals.

A small series of cases was presented in which the metabolism was studied before and after treatment with a modification of Ringer's solution suggested by Loeb. Variable results were obtained. In some instances more base than acid was retained, and in other cases the reverse took place. The conclusion was drawn that saline alone could not be relied on to combat acidosis.

The observations made in severe diarrhea indicate that there is a loss of electrolyte which cannot be attributed to loss of blood plasma or of intercellular tissue fluid alone. The large amount of potassium lost indicates that intracellular fluid is lost in considerable quantity. A comparison of potassium and nitrogen retention shows that loss of potassium is seldom accompanied by a proportionate loss of nitrogen and may even be accompanied by retention of nitrogen. The conclusion is drawn from this that intracellular fluid may be lost without death of cells. Hitherto, attention has been directed only to the replacement of plasma electrolyte and that of intracellular tissue fluid. The question of replacing intracellular fluid appears of equal importance, and should by no means be neglected.

DISCUSSION

DR. OSCAR M. SCHLOSS: Since Howland and Marriott first demonstrated the occurrence of acidosis in severe diarrhea, numerous investigators have sought evidence that would throw light on the mechanism by which the acidosis is produced.

Dr. Holt's figures are the first to show loss of base in severe diarrhea. A continued greater loss of base than loss of acid would undoubtedly be sufficient to cause severe acidosis. Despite Dr. Holt's convincing figures, I am still reluctant to accept this as the only cause of the acidosis. Indeed, Dr. Holt stated that he did not consider it the only possible cause. If it were, then I should feel that the

plasma in cases of acidosis with diarrhea should show regularly a diminution of total base. This is not the case. Although the base may be reduced in some cases, this reduction occurred in only a small number of those recorded by Hamilton, Hartman and Hoag.

Since the work done in collaboration with Dr. Harrington in 1916, I have been strongly impressed by the relationship of the secretion of urine to the acidosis which occurs in dehydration. Oliguria or anuria occurs almost regularly when the acidosis is severe, and the establishment of normal secretion of urine by the proper employment of solutions of salt and dextrose is followed regularly and often promptly by relief from acidosis.

I do not wish to minimize in any way the importance of Dr. Holt's demonstration of loss of base in diarrhea, but I think that the failure of the kidney to eliminate acid and to conserve base should not be lost sight of as a significant factor.

DR. L. A. HOAG: It is true, as Dr. Holt has pointed out clearly, that there are different methods in which acidosis may result during the course of diarrhea and dehydration. Previously, these have been demonstrated chiefly by the analyses for plasma. Dr. Holt is the first to have analyzed carefully data which make it possible to study the true balance of mineral substances in diarrhea.

It is evident that more fixed acid than base is excreted in the urine of normal infants. This proportion holds true also during the development of diarrhea, but the total amount of each, particularly that of the chlorine, decreases, resulting in a marked diminution of acid excretion. The predominance of base over acid in the stools is not much greater in severe diarrhea than in the normal state (1.81 : 1 compared with 1.74 : 1). The retention of acid because of oliguria and the loss of base because of loose stools combine to give the relative and absolute loss of base which Dr. Holt has emphasized.

In severe diarrheas the total amount of base and acid excreted always exceeded that which was taken in through the mouth. This loss must have been derived from the body, as Dr. Holt has shown by the special analyses of his data. Extracellular fluid and plasma must have been the direct origin of this loss, because the chemical substances involved could have reached the kidney and intestines only through the circulating plasma. In this connection one must remember that in plasma the proportion of fixed base to fixed acid is nearly 1.5 : 1. If one plots the total excretion from the body in the normal infant it shows a preponderance of 1.09 parts of base to 1 part of acid. If one adds to that the base and acid being lost from the plasma in the proportion of 1.5 to 1.0, it tends to build up steadily the preponderance of base over acid without necessarily changing particularly the relation of base to acid in the blood left in the body. I do not mean to give the impression that the addition of such plasma fluids can account for, in their entirety, the changes in total excretion demonstrated by Dr. Holt, but to call attention to one of the many factors that have to be considered.

The data presented to show the variable effects on mineral balance induced by the parenteral use of Loeb's solution might be more readily interpreted if the changes in the volume of urine were considered. I say this because of the demonstrated fact that the production of distinct diuresis removes large amounts of retained acid from the body. On the other hand, if the quantity of fluid used was relatively small and the volume of urine showed little increase, no constant effect on acid-base balance need be expected.

THE TREATMENT FOR ANEMIA IN INFANCY. DR. HUGH JOSEPHS.

I shall present a few cases illustrating the possible effect of copper in the cure of anemia in infancy. These cases do not comprise a controlled series, but merely point to a possibility that copper given in addition to iron may have some effect. For my own convenience, I have divided the cases into three groups: anemia due to prematurity, anemia due to infection and anemia that was apparently of nutritional origin.

So far, anemia of prematurity has not been studied except in so far as the effect of giving iron is concerned. Our work on anemia due to infection and anemia dependent on nutrition is not finished. In order to draw definite conclusions, one needs enough cases for statistical study, and these I have not yet obtained. However, enough has been done to permit of very suggestive inferences.

Iron was given as a 10 per cent solution of ferric-ammonium citrate, 2 cc. per kilogram of body weight. The copper was given as a 0.5 per cent solution of copper sulphate, 1 cc. per kilogram of body weight. That is a large dose of copper; I think that possibly a smaller dose would give results and I am trying smaller doses now. Both iron and copper were given together in milk. I have not attempted to give copper sulphate by itself. I have not seen any untoward results from the use of copper when given in the milk.

The first case was in a baby who was about 4 weeks of age at the start of the experiment. The child had had jaundice at the age of 2 weeks. Following the jaundice the hemoglobin was found to be about 45 per cent. There was probably an infection to account for this. The administration of iron was started as soon as the temperature had been normal for a week. Almost immediately the hemoglobin began to rise, and after twenty-five days it reached 80 per cent.

The second case was somewhat more interesting though similar. Jaundice occurred at 2 weeks of age; the hemoglobin was 45 per cent. Iron was given for eleven days but had no effect except on the reticulocytes. As soon as the copper was given, the hemoglobin rose rapidly and had reached 70 per cent at the end of fifteen days.

The third case was that of a child, aged 18 months, who had a nutritional type of anemia. Iron began to have its effect after a period of five days. The reticulocytes rose, and the hemoglobin increased with fair rapidity.

I included this and the first cases because they more or less acted as controls. I did not want to give the impression that I have not had any good effect with iron alone.

The fourth case is that of a child with pneumonia, in whom following the crisis the hemoglobin was found to be about 45 per cent. Iron was given after a period of ten days; the temperature was normal, and the hemoglobin rose rather slowly until copper was given, after which there was a rapid rise in hemoglobin to about 70 per cent.

The next child was observed for seven or eight days on a milk diet alone, during which time the hemoglobin remained at 40 per cent. We then gave iron. After five days there was a rise in the hemoglobin to 55 per cent, where it stayed for two weeks although the dosage of iron was doubled. Then copper was given, and an immediate rise to over 70 per cent took place. At this point an infection occurred, and the hemoglobin dropped to 55 per cent and remained there until the infection cleared up. It then rose almost as quickly to 70 per cent again.

In two cases I gave iron and copper at the same time as soon as the children were admitted. In the first case a rise occurred about as much as in my first case in which iron alone was given. In the second case the child came in with hemoglobin of 24 per cent and was given iron and copper together; within twenty days from the beginning of treatment the hemoglobin was about 70 per cent.

These results with copper were somewhat surprising. I did not expect them and do not know what to make of them. More controls are needed before I can draw any conclusions as to the effect of copper in the treatment for anemia. The results thus far have tended to confirm the results in the anemia of rats as first obtained in Steenbock's laboratory. In a number of cases I can say definitely that the hemoglobin formation was accelerated by the use of copper.

DISCUSSION

DR. MARTHA WOLLSTEIN: At the Babies' Hospital we use iron in some cases, liver in other cases and liver and iron combined in others. The majority of the cases that we are studying come under the classification of the nutritional anemias;

that is, anemia that is due to the exhaustion of the iron reserve with which the infant is born and to which he has not added by proper food, the food having been chiefly milk. This anemia develops earlier in premature infants than in full term babies, and earlier in twins than in single babies. The type, however, is the same.

It has been found by many observers that in the second half of the first year the normal infant develops what Baar termed physiologic anemia. From our studies of the blood of the infant throughout the first year we know that it is in the second half of the first year that the red cells and the hemoglobin are lower than at any other time. At the beginning of the second year, both rise under the influence of the more mixed diet, etc.

The infants that we have treated with iron alone have shown a marked increase in reticulocytes within a week.

One case showed a rise of hemoglobin from 34 to 71 within three weeks on iron alone. We used albuminate of iron or the citrate. With iron alone the children showed half as large an increase of reticulocytes as did the children who were treated with iron and with liver. In some of those cases, the reticulocytes rose to 8.6 per cent. In one infant the hemoglobin rose from 22 to 74 in five weeks.

It takes longer to obtain improvement in a case of anemia in which the hemoglobin is as low as 23 than it does in less marked cases in which the hemoglobin is over 35.

The patients treated with liver and iron showed a much more marked rise than did those treated with liver alone, or with iron alone.

The addition of liver also increases the appetite markedly and increases the weight more rapidly than is the case when iron alone is given.

We have not treated any children with copper directly but in the light of the most recent work from Wisconsin, where Steenbock and his co-workers found that copper is apparently the active principle in liver, perhaps in feeding liver we are doing just what Dr. Josephs is doing.

The liver is taken well by the children. It stimulates the appetite, increases the weight and increases the reticulocytes and hemoglobin.

DR. JOSEPHS: I have treated children with liver and can confirm Dr. Wollstein's results not only in this type of anemia but in one or two of the anemias in prematurity when the hemoglobin was raised somewhat but not as much as I had hoped.

It is hard to say whether it is the copper in the liver which is the important factor. This is a point about which there is a great deal of controversy going on. Perhaps the copper in the inorganic form is the thing that stimulates the reticulocytes. I think it is the inorganic iron that is important in the iron given in food, although from the iron in food one might expect a rise, but a slower rise.

CHANGES IN SERUM ELECTROLYTES IN RICKETS. BENGT HAMILTON.

The present work was carried out on rabbits that had been made rachitic on the McCollum diet no. 3143. The purpose of the work was to find out whether in rickets the decrease in phosphorus is the only change in the serum. There was reason to believe that the decrease in phosphorus was not an isolated phenomenon.

Before the hypodermic injection of phosphorus the serum phosphorus was very low and the calcium normal. After the injection the phosphorus increased and the calcium dropped. The same phenomenon has been demonstrated by other investigators in normal animals and also in patients. Holt demonstrated it in a rachitic infant.

The fact that the amount of calcium decreases can most plausibly be explained thus: Both in rickets and in the normal condition the serum is saturated in respect to calcium and phosphorus. If, however, two solutions, both having the same concentration of calcium, but one a much lower amount of phosphorus, both

are saturated in respect to calcium and phosphorus, then the chemical properties of these solutions cannot be the same.

The bicarbonate values of fifty-seven rachitic and twelve normal rabbits have been computed against the chloride values. If they are all taken together, there is no correlation between bicarbonate and chloride. If, however, the cases are grouped according to their phosphorus values, then it may be seen that in each group there is a definite correlation between bicarbonate and chloride. It may also be seen that when the phosphorus decreases, the relation between bicarbonate and chloride undergoes a change. Most of the highest values, both of chloride and bicarbonate, are found in the rachitic animals.

As to the quantitative relationships it may be calculated that a decrease of phosphorus of 1 mm. corresponds to an increase of chloride or bicarbonate of about from 5 to 10 mm. This shows that the high chloride and bicarbonate values found in cases with very low amounts of phosphorus do not represent the substitution of one acid for another, nor can it be a matter of osmotic compensation. It is possible that this relationship between chloride, bicarbonate and phosphorus in rickets may have some bearing on the seemingly paradoxic fact that in rickets the serum is saturated with calcium phosphate.

DISCUSSION

DR. BENJAMIN KRAMER: In the study of rickets, we found two types of cases: that of the child who has a very low phosphate and a normal or moderately reduced calcium value and that of the child who has a low calcium value with a low normal inorganic phosphorus value in the serum; the latter child has rickets plus tetany with a normal or reduced amount of phosphate. When calcium is given to a child with tetany, the calcium returns to normal and the phosphate concentration of the serum drops, but the product of these values remains the same.

The reverse of this occurs in animals following the injection of phosphate; i.e., the serum calcium level declines. If rachitic children are given phosphate by mouth, the same phenomenon occurs as in rabbits. It was this phenomenon which led us to consider that solubility product relations may play a part in calcification. However, these phenomenon are not observed in children if, along with the calcium or phosphate, cod liver oil or some other antirachitic agent is administered.

One fact that we have been unable to explain is the different calcium phosphorus product level obtained in the rachitic child as compared to the normal child. That is, in the rachitic child with tetany, the administration of calcium raises the calcium but lowers the phosphate so that the calcium phosphorus product remains unchanged, but in normal children this product is maintained at a constant but higher level; possibly the total ionic strength of the serum plays a part.

Studies on calcification in vitro have shown that there are other factors besides calcium and phosphate concentration in serum that play a part in calcification. One of these is the reaction. As the reaction approaches neutrality, calcification fails to take place even though the product is adequate. The total ionic strength of the solution is another factor.

In the experiments that Dr. Hamilton has reported, he has demonstrated for the first time that the concentration of electrolytes other than calcium and phosphate may play a part in calcification in vivo. In human beings, as far as I know, no changes in the total ionic strength of the serum have heretofore been demonstrated which would materially influence calcification. Calcium phosphorus products greater than normal have been observed in renal rickets. It is possible that a large part of the calcium here is un-ionized.

EARLIEST ANATOMIC CHANGE IN RICKETS. EDWARDS A. PARK.

The following experiments were performed by Dr. Martha Eliot of the Pediatric Clinic of Yale University, Miss Deborah Jackson of the Pediatric Clinic of Johns Hopkins University and myself.

One hundred rats, aged 6 weeks, were placed on the Steenbock rickets-producing diet. Fifty were let alone, and constituted the experimental animals; fifty irradiated with the quartz lamp for five minutes daily were the control animals. Groups of the experimental animals and corresponding groups of the control animals were killed on the first, second, third, fourth, fifth, seventh, eleventh, fourteenth, twenty-first, twenty-ninth and thirty-fifth days of the experiment; the pooled blood was analyzed for calcium and phosphorus; the tibiae were studied histologically. X-ray pictures of the tibiae were made at weekly intervals throughout the experiment, and also after the animals were killed. Moreover, pairs of animals, one an experimental and the other a control animal, were killed between the times mentioned to be studied histologically, so that it might be possible to trace the development of rickets from day to day.

As the result, we were able to obtain interesting correlations between the histologic development of rickets, the changes in the calcium and phosphorus levels of the blood and the growth of the animals through measurements obtained from the x-ray plates, and we were able to compare these data with the same data in the control rats prevented from developing rickets by ultraviolet irradiation.

At the end of the first week on the rachitic diet a broadening of the proliferative cartilage was demonstrable in the x-ray pictures of the experimental animals as compared with the controls. The x-ray pictures of thirty experimental and thirty control rats were available for study. This broadening of the cartilage was also apparent, as determined by measurement, in the histologic preparations from the three experimental rats killed at this time. At the end of the first week, when this broadening of the cartilage appeared in the experimental rat, lime salt deposit was everywhere present in the provisional zone of calcification, but was more delicate than in the control rats and did not extend so far into the cartilage. The calcium level in the blood of the experimental rats was 10.5 mg. per hundred cubic centimeters of blood, and in the control rats 11.6 mg. The phosphorus in the blood of the experimental rats was 5.5 mg., and in the control rats 6.9 mg. The product of the calcium $\times$ phosphorus in the experimental rats was 58, and in the control animals 80. Probably in the experimental animals the osteoid tissue in the shaft and center of ossification was a trace more abundant than in the controls. But it was difficult to be certain of this fact.

At eleven days the cartilage in the experimental animals was still broader than at seven days and much broader than in the control rats at eleven days. Calcification of the provisional zone of cartilage was everywhere present but was extremely thin and extended in many places only one cell or less deep into the proliferative cartilage. The lime deposits had become so thin that breaks seemed imminent. In the control rats, in contrast, the lime salt deposit was heavy and extended from 2 to 4 cells deep into the proliferative cartilage. The extension or mounting upward of the shaft along the side of the proliferative cartilage had begun posteriorly. The line of division between cartilage and shaft remained sharp, but showed irregularities because the cartilage was broader at some points than at others. In the control rats the cartilage-shaft junction tended to be even. Osteoid tissue in the center of ossification and the shaft was slightly more abundant in the experimental rats than the controls but did not seem more abundant than is sometimes seen in growing rats considered healthy. At this time (eleven days), the calcium in the experimental group was 12.5 mg. and the phosphorus was 4.5 mg. The calcium $\times$ phosphorus product was 56 mg. The blood from the control animals was lost.

At fourteen days the cartilage had become still broader in the experimental rats. The broadening was greatest in the middle and least anteriorly (the sections of the upper end of the tibia were made from before backward). At the broadest point the measurement was almost twice that in the control rats. The line of division between cartilage and shaft was still definite, and calcification was present except for a few gaps here and there, not more than 2 or 3 cartilage cells wide. Where present, it was exceedingly delicate and, in the plane of the microscopic section, seemed fragmentary. It did not form a continuous network with the

main strands or branches parallel to each other in the longitudinal direction of the bone as under normal conditions and as so well shown in the slides from the control animals. No invasion had taken place. The osteoid tissue was definitely increased. The structure of the trabeculae in the shaft just under the cartilage was irregular in places and there reflected the slight irregularity in the cartilage cells and also the lightness and imperfection in the lime salt deposition. At this time (fourteen days), the calcium in the blood of the experimental animals was 11 mg. and in the control animals 12.6 mg. In the experimental animals the phosphorus was 3.9 mg., and in the control animals 5.9 mg. The calcium × phosphorus product was 43 in the rachitic animals and 74 in the control animals.

By twenty-one days rickets was exceedingly marked. Extensive invasion of the cartilage through some of the parts undefended by calcium had taken place, the osteoid was well developed and the picture of advanced rickets with which we are all familiar was everywhere in evidence. The calcium in the experimental animals was now 12 mg., and in the control animals 13.6 mg. The phosphorus in the experimental animals was 3.4 mg., and in the control animals 5.9 mg. The calcium × phosphorus product in the experimental animals was 41, and in the control animals 80.

The interesting features brought out by this study I can allude to briefly. The first clearly demonstrable change in the rachitic animals was a broadening of the proliferative zone of cartilage, particularly in the middle portion. Where present, this broadening process seemed to involve all zones of the cartilage. It was most prominent, however, in the middle zone of medium sized round cells and in the zone of very large cells which lies next the shaft. Obviously, under the influence of the rachitic conditions imposed on the animal, the evolution of the cartilage cell had been slowed from the time when it was first formed at the beginning of the proliferative zone to the time of its meeting with the shaft, and its assimilation by the shaft had been rendered more difficult or else the assimilating power of the shaft had been impaired. Apparently this delayed assimilation of the cartilage cell is more marked in the cartilage lying in the central portions of the bone than at the extreme sides, a phenomenon which is one of the factors in the production of cupping.

It is wrong to think that this broadening of the cartilage preceded all other developments of rickets, for hand in hand with this broadening of the cartilage went a failure in the lime salt deposit. But this failure is much more gradual and even than we had supposed. We had thought that at certain points in the proliferative cartilage for some unknown reason the deposition of calcium stopped, whereas at other points it continued much as under normal conditions. In reality in this experimentally produced rickets, the lime salt deposition progressively became thinner and thinner, until at various points it stopped altogether.

Osteoid formation also gradually occurred, so gradually that at the end of eleven days it was perhaps in excess of that normally present in growing animals, and at the end of fourteen days it was clearly in excess.

Various students of rickets have thought that the breadth of the proliferative cartilage meant that in the disease there was a more rapid production of cartilage cells than normal. This was the view, for example, formerly expressed by Ziegler. The present experiments furnish, so far as I am aware, the first reliable proof that the theory mentioned is incorrect, for measurements showed that the actual growth in length of the tibiae and of the animal as a whole was slightly superior in the control rats receiving ultraviolet therapy and showing no broadening of the proliferative cartilage.

We had expected to find that the rats showing the greatest broadening of the proliferative cartilage would be those animals which grew most rapidly. Obviously, if no growth takes place in the animal, there can be no rickets and, also, the faster an animal actually having rickets grows, the greater will be the rickets. The data furnished by these experiments in regard to this particular point are so few that no conclusions are possible. They suggest, however—and I believe that further experiments will prove—that in the rat on a given rickets-producing diet, the

greater the degree of rickets, the poorer the growth of the bone in length will be. As a matter of fact, this result is exactly what we should expect, namely, that the organism least affected by abnormal environmental conditions will exhibit the best growth and that the organism most affected by the adverse conditions will be most affected, also in point of growth.

It remains to be seen to what extent these observations made on the rat apply to the problem of rickets in the human being.

DISCUSSION

DR. PAPPENHEIMER: In studying the earliest rachitic change in the experimental animal, and in correlating the anatomic lesions with the alterations in the blood calcium and inorganic phosphorus, Dr. Park and his collaborators have filled a definite gap in our knowledge of the disease.

I agree with Dr. Park that there is little evidence of increased multiplication or growth of cartilage cells in rickets; the excessive width of the cartilage is probably due rather to the lessened destruction of the cartilage cells by the blood vessels of the marrow. It has seemed to me that the deposition of new calcium in the matrix of the cartilage ceases almost from the moment that the animal is placed on the rickets-producing diet. The calcium already deposited in the preexperimental period is gradually pushed downward toward the shaft by the continued growth of the basal layers of cartilage cells, and is still evident, as Dr. Park has shown, during the early period of the disease. Gradually, however, it is reabsorbed, more rapidly, perhaps, in the central portion of the cartilage than at the edges, where remains of the calcium persist even after three or four weeks. Since the calcification of the matrix is essential for the orderly destruction of the cartilage cells at the epiphyseal lines, its disappearance means that the unopened cartilage cells are pushed downward toward the shaft by the continued, but not necessarily accelerated, growth of the basal layers of cells. In this way arises the broadened, calcium-free and often irregular cartilage characteristic of the rachitic bones. It is interesting to note that the rachitic lesions can be detected histologically while the inorganic phosphate of the blood is still within the normal range.

PHILADELPHIA PEDIATRIC SOCIETY

JOHN D. DONNELLY, M.D., *Reporter*

Stated Meeting, Jan. 14, 1930

RALPH M. TYSON, M.D., *President, in the Chair*

A CASE OF STILL'S DISEASE. Presented by DR. EDWARD L. BAUER.

Arthritis deformans with lymphatic hyperplasia in children is referred to as Still's disease. Etiologically, there is no reason, so far as is known, for considering Still's disease as a separate disease entity. Clinically and pathologically, there is much evidence to link this disease with arthritis deformans.

Charles van A., about February, 1929, began to complain of pains in his head and chest accompanied by malaise. Later, he complained of pains in his joints but was able to walk about. In July, he became bedridden with marked involvement of the joints. He was given sodium salicylate and later a course of *Streptococcus immunogens*, after which he seemed worse. The family history was unimportant. His previous medical history included only an attack of measles.

Physical examination made at the Jefferson Hospital showed an anemic lad 4 years of age, without tonsils and adenoids but with an infection of the ethmoid sinus and involvement of the frontal sinus. The cervical and inguinal glands were

enlarged, and the axillary and epitrochlear glands were markedly enlarged. The heart, lungs and abdomen showed no pathologic processes. The wrist, the metacarpophalangeal and the proximal phalangeal joints of the upper extremities were symmetrically enlarged. They were not red or tender, or unduly warm, but the surrounding tissue appeared thickened and there was a sense of fluctuation in the larger joints. The knees and joints corresponding in the foot to those of the wrist and hand were similarly involved, with limitation of motion.

Blood counts showed: hemoglobin, 40 to 46 per cent; red blood cells, 3,150,000 to 3,275,000, and white blood cells, 12,300 to 12,900. The differential picture was normal. Chemical analysis of the blood gave: sugar, 86 mg.; nonprotein nitrogen, 27.02 mg.; calcium, 9.54 mg., and phosphorus, 4.98 mg. The Wassermann and Kahn reactions were negative. Cultures from the nose and the sinuses showed *Staphylococcus aureus.* Throat culture showed *Staphylococcus aureus, Streptococcus viridans, Micrococcus catarrhalis* and diphtheroid bacillus. Examination and culture of the stools gave normal results. Repeated urinalysis showed faint traces of albumin and from occasional to moderate amounts of pus, but no sugar, blood or casts.

Roentgen examination showed a considerable amount of exudate in the joints of the fingers, wrists, feet, ankles and knees, but no evidence of bone destruction at any joint. The lesion appeared to be primarily a synovitis. There was considerable decalcification of all long bones and those of the hands and wrists, which should be expected to occur after disuse and multiple joint lesions. The joint swellings may have been due to the greatly swollen membrane rather than to extensive exudate. There was no evidence of epiphysitis. There was some slight cloudiness of the anterior ethmoids and of the right maxillary antrum. The other accessory sinuses were normal.

The synovial fluid was scant and sterile. Pathologic examination of an axillary gland showed a simple hyperplasia. A companion gland was cultivated and showed a diphtheroid bacillus resembling, but not identical with, a diphtheroid bacillus recovered in Hodgkin's disease. Later, another gland was removed, with all sterile precautions taken, and the same organism was recovered.

The patient showed a marked improvement following the use of an autogenous vaccine made from the discharge from the ethmoidal sinus.

INTRACRANIAL HEMORRHAGE OF THE NEW-BORN. Presented by DR. RALPH M. TYSON and DR. WILLIAM H. CRAWFORD.

A study of forty-five cases of cerebral hemorrhage was presented. The incidence of hemorrhage among 2,256 deliveries was 1.9 per cent. Of the stillborn infants that came to postmortem examination, 32.1 per cent had hemorrhage. After discarding the questionable cases, it was found that 35.5 per cent of the infants with hemorrhage had recovered.

The classic symptoms of hemorrhage were: a history of difficult delivery, difficult resuscitation, fretfulness, inability to nurse and swallow properly, intermittent cyanosis, muscular twitchings, excessive loss of weight, fever within the first two days and increased intracranial pressure with bloody fluid.

Intracranial hemorrhage was found in infants delivered spontaneously, by forceps, version and breech extraction; in rapid, precipitous deliveries and in prolonged and difficult labors. The authors were unable to determine the size and location of hemorrhage by clinical methods. Postmortem examination showed that a large proportion of the hemorrhages occurred in the basal areas. In the fatal cases, nearly all infants died within forty-eight hours. For controls, drainage was done in sixty-six normal patients which gave an average spinal pressure of 8 mm. of mercury, bloody fluid in fourteen cases, yellowish fluid in thirty-two cases and clear fluid in twenty cases. Treatment consisted of careful nursing and feeding, gavage when necessary, quiet and rest, stimulation, and repeated drainage for relief from pressure symptoms.

From their experiences, the authors concluded: 1. Long second stage of labor, precipitous delivery, and difficult obstetric procedures are the chief causes of intracranial hemorrhage. 2. Prenatal health of the mother and hemorrhagic disease of the new-born are not important causative factors. 3. History of the delivery, clinical symptoms and lumbar or cisternal puncture are the essential points of diagnosis. 4. Repeated drainage of the spinal fluid with relief from increased pressure is a most valuable means of treatment. Equally essential is good nursing and feeding care. 5. Preventive measures consist in skilful obstetric procedures, the use of carbon dioxide and oxygen for resuscitation and the transfusion of whole blood intramuscularly in all cases of possible hemorrhage.

DISCUSSION

DR. IRVING WOOLMAN: I have brought with me two heads of infants that show intracranial hemorrhage. The hemorrhages in these two cases were due to tentorium tears. Ninety-five per cent of all intracranial hemorrhages in the new-born are due to this cause. At autopsy, the dura mater is often found intact. One of the babies with such a condition lived less than ten hours, the other lived five days.

DR. RALPH M. TYSON: Intermittent cyanosis is a prominent symptom, but it may be confused with the cyanosis occurring in certain new-born infants in whom oil drops, containing menthol, have been instilled in the nose. A cyanotic attack so developed closely resembles that due to intracranial hemorrhage. Involvement of the phrenic nerve is another point in differential diagnosis that is occasionally found in infants delivered with difficulty and in whom arm birth palsy is present. This symptom means a paralysis of the diaphragm that causes a marked respiratory disturbance, in which cyanosis occurs at intervals, and in which the infant is a picture of distress, not unlike the distress due to intracranial hemorrhage. I have had three such patients; two of them died and the other one made a complete recovery. In those cases, the spinal fluid was negative, the sucking reflex not disturbed, and there was uneven expansion of the chest, rapid and jerky respirations, and signs of an unexpanded lower lobe on the side involved. Under the fluoroscope, the diaphragm on the affected side was high and motionless, and a to and fro motion of the heart was noted. An effort is being made to follow these infants and watch their development. Pictures were shown of some infants who had recovered from intracranial hemorrhage.

CLINICAL AND BACTERIOLOGIC STUDIES IN PYELITIS IN INFANTS AND CHILDREN. Presented by DR. MYER SOLIS-COHEN.

Most of the theories in regard to the etiology, pathogenesis and treatment of pyelitis are based on ordinary cultures of the urine. Dr. Solis-Cohen has frequently shown, and others have confirmed this, that when simultaneous cultures are made on ordinary mediums and in the patient's fresh, whole, coagulable blood, organisms growing on the former are absent in the latter, and vice versa. Organisms able to grow in a person's blood are believed to be pathogenic to him, while those unable to survive in it are regarded as nonpathogenic to him.

The colon bacillus, so frequently found in ordinary cultures of urine in cases of pyelitis and hence often regarded as the etiologic factor, fails to grow in the patient's blood in many cases, while staphylococci or other pyogenic organisms not present or in small numbers on ordinary culture of the urine, do grow when the urine is cultured in the patient's whole blood. In such cases similar pyogenic organisms are usually also found in the upper respiratory tract, indicating that the pyelitis is probably secondary to an infection of the upper respiratory tract. The pyelitis cannot be cured until the diseased tissue in the upper respiratory tract has been removed and the patient's resistance to the infecting organism raised artificially by careful administration of a pathogen-selective vaccine that contains the proper antigen and is usually extremely potent.

DISCUSSION

DR. MYER SOLIS-COHEN: In response to the question as to how to cultivate anaerobes, Rosenow's brain medium is used because most organisms grow in it. I do not consider this medium a strictly anaerobic culture medium. In my work with Heist on globoid bodies a real anaerobic jar was devised. The technic has varied. The early cultures were made on Löffler's medium, then bouillon was used, then beef heart and brain medium, whereas the last hundred or so cultures have been made with Rosenow's brain medium. In many cases, when the urine was cultivated in Rosenow's brain medium, *Bacillus coli* grew alone or in greatest numbers, with staphylococci or other pyogenic organisms growing less profusely. But when this same urine was cultivated in the patient's own blood, only the staphylococcus grew, the colon bacillus having disappeared entirely.

TETANY OCCURRING IN IDENTICAL TWINS AT EIGHT WEEKS OF AGE. Presented by DR. EDWARD D. ATLEE.

Tetany is unusual before the age of 4 months. Hill cites a case reported by Wolff in which tetany occurred in an infant, 7 weeks of age. Several cases are reported in the literature as occurring as early as 6 weeks. Bakwin, Bakwin and Gottschall, in their recent paper on the comparison of various treatments for tetany, mention one case which occurred at 6 weeks, one at 8 weeks and one at 9 weeks.

B. S. and V. S., twins, were born of a healthy primiparous negress in whom the Wassermann test of the blood was negative. The infants appeared to be probably two to three weeks premature. Both cried lustily immediately after birth and appeared normal. One weighed 3 pounds and 15 ounces (1.78 Kg.); the other, 4 pounds and 2 ounces (1.87 Kg.). They were treated as premature because of their size. They were girls and identical, there being but one placenta. Wassermann examination of the cords gave negative results. The infants were given skimmed lactic acid milk on the second day, with a little breast milk added occasionally. The mother's breasts were poorly developed, and the secretions soon dried up. After seven weeks the patients were considered strong enough to send home, as their growth had been satisfactory and their progress uneventful. At this time their diet consisted of 3 ounces of whole lactic acid milk, third hour, seven feedings per day; 1 ounce of orange juice and 15 drops of cod liver oil. The cod liver oil was started at 6 weeks of age. On discharge from the hospital, physical examination gave negative results.

Nine days after discharge, the smaller twin was returned with the following history: Shortly after returning home, both infants developed acute nasal infections with profuse discharge. The previous day, the smaller twin had vomited her feeding and cried as if in pain. When she was returned to the hospital the next day, generalized twitchings and convulsions developed. She weighed 6 pounds and 3 ounces (2.81 Kg.), and she was extremely hypertonic, with frequent convulsive seizures produced by the slightest jarring. There was a profuse nasal discharge, sluggish pupillary reflexes, reddened pharynx, distended abdomen and small, tympanitic, umbilical hernia and exaggerated reflexes. Chvostek's and Trousseau's signs were not elicited, but carpopedal spasm was present. Otherwise the examination gave negative results.

Three days later the larger twin was admitted to the hospital in a similar condition, with the same history and physical signs.

Active antitetanic therapeutic measures were instituted at once, with daily intramuscular injections of three units of parathyroid extract-Collip for seven days and 3 cc. of calcium gluconate for three days, together with heliotherapy and viosterol. The nasal infection received prompt treatment. After ten days all twitchings had ceased; however, both babies were hypertonic. At the end of three weeks they were sent home in good condition. Roentgen examination of the long bones showed generalized and widespread evidence of rickets in the early stage. The smaller twin after admission received breast milk exclusively for four days,

with a definite improvement in symptoms. She was then put on a regimen of lactic acid milk. The larger twin received a mixture of both breast and lactic acid milks for three days, with some improvement; then she was given only lactic acid milk.

CHICAGO PEDIATRIC SOCIETY

Clinical Meeting, Jan. 21, 1930

A. H. PARMELEE, M.D., *President*

SITUS TRANSVERSUS. DR. WILLIAM L. BUHRMAN.

This colored girl, aged 6, complained, on entrance, of insomnia and a difficulty in breathing of about six months' duration. Her mother stated that she had snored and had been a mouth breather since birth.

She had whooping cough at 2 years of age, measles during the summer prior to presentation and frequent colds with a temperature of varying degrees.

Examination revealed markedly hypertrophic tonsils, liver dulness on the left, and cardiac dulness extending to the right of the sternum. Her pulse rate varied from 64 to 70 and was irregular, especially after exercise. There were no murmurs.

Roentgenographic examination showed the stomach on the right side and typical congenital transversus cardia.

The electrocardiogram showed a typical mirror image in lead; and incomplete heart block; a month later a sino-auricular block was found on re-examination.

During her stay in the hospital she had one attack of acute tonsillitis, during which her temperature reached almost 105 F.

I believe that the partial heart block is due to one of the rheumatic types of infection, even though a congenital anomaly exists. True congenital heart block is comparatively rare. There are only thirty cases on record, about twenty of which have been recorded since 1923. Most of the infectious cases are due to diphtheria and rheumatic fever.

TWO CASES OF STRIATAL SYNDROMES IN BOYS. DR. PETER BASSOE.

CASE 1.—These two boys were each aged 7 years. The first one was the result of a normal delivery. It was noted that he had a squint almost from birth, and a tendency to nocturnal enuresis. He was otherwise normal until about 1927, when the family went on a trip in the Rocky Mountains. At that time it was noticed that he began to drag the right leg, and in a few weeks he began to have incoordination of the right leg. He was taken to a hospital in St. Louis, where chorea was suspected. After a time he began to jerk in the left side also. A lumbar puncture showed normal fluid. During the next year there was some temporary improvement, but in 1929, new symptoms set in, particularly disturbance of speech, which persisted.

He came here in October, 1929, and the condition had not changed much, although perhaps he used the extremities a little better. The tongue was not protruded well and it deviated to the right. It was rather flabby and tremulous. At rest there was not much tremor, but on movement there was marked tremor of the extremities. Any attempt to grasp anything with the hand was likely to bring on a generalized tremor.

The deep and superficial reflexes were normal. There was no real paralysis, except that the right hand was slightly paretic. The difficulty in the use of the extremities was mainly in coordination. At times there was a slight nystagmus.

I did not make a positive diagnosis. There was no familial tendency to anything similar. There was no question that he had choreic movements, but he had more than chorea. It was probably some form of encephalitis, and I believe

that the epidemic form should be considered first, although this is not a typical case, but it may be some other type of infection.

CASE 2.—This boy of the same age also had trouble chiefly with the right side. The birth was normal. He had nondescended testicles, so that both these children had some stigmas of constitutional inferiority. This boy was said to have been quite well until July 19, 1929, when he was struck by a motor driven vehicle and was taken to Cook County Hospital. He had a wound at the back of the head. Some weeks later when he left the hospital it was noticed that he had slow, peculiar, jerky movements of the right arm and the face and lagging of the leg. This tendency to hypermotility remained.

When I saw him in October he had been back in school but could not remain quiet and was brought to the Presbyterian Hospital. At that time the athetoid movements in the right hand were more definite than now. His tongue also deviated a little to the right and as he protruded it, it showed a tendency to rhythmic movements. When he was first seen I could not get him to talk but he talked occasionally at the time of presentation. There were practically no changes in his reflexes. He could walk with difficulty. There was nothing abnormal in his eyegrounds or in the spinal fluid.

From the standpoint of sypmtomatology, without knowing anything about the history, one would say that here also is a case in which extrapyramidal symptoms predominate. The symptoms are best explained by assuming lesions in the basal ganglia. According to the history he was well before the injury, so the question is raised as to whether it is possible for an injury to the head to produce such a syndrome. I would say that it is possible but not probable, for we have a picture which ordinarily is looked on as some form of encephalitis. However, in rare instances we meet with traumatic choreo-athetosis as well as traumatic parkinsonism.

MALARIA IN INFANT (DUE TO TRANSFUSION WITH INFECTED BLOOD). DR. ELEANOR LESLIE.

A boy, aged 18 months, had been premature. His history was uneventful until the summer of 1929, when he was taken to the Daily News Sanitarium with a history of fever for several weeks. Dr. Crane saw the child and sent him to the hospital, where definite observations were made of right-sided empyema. On aspiration thick, greenish pus was obtained, which showed *Streptococcus viridans*. The pus was so thick it could not be aspirated well. On August 27, Dr. Gatewood put in a single tube and established negative drainage. The patient did well for a few days and then developed a temperature which ranged from 98 to 106.5 F. A blood culture showed a few colonies of *Streptococcus viridans*. The hemoglobin of the patient's blood dropped to 29 per cent and his general condition was so bad that it was thought best to give a transfusion. On September 11, we gave 100 cc. of his father's blood in the jugular vein. There was immediate improvement but within a few days the hemoglobin, which had risen to about 60 per cent following transfusion, fell to 40 per cent. Examination of a smear showed very pale red cells.

About October 18, the child had a sudden rise of temperature to 103 or 104 F. When the temperature receded he apparently felt well. Dr. Needles in examining the blood smear found what he thought to be malarial parasites but he was not sure. The blood smear was then examined by Dr. Pernokis who was sure of the parasite. We had given another transfusion before we were sure it was malaria.

The boy's father lived for fourteen years in Greece in places where the quartan malaria is very prevalent, and examination of his blood showed malarial indications.

Quinine therapy was employed and the child made a rapid gain and marked improvement in every way. The administration of quinine was stopped on December 5th, just before the patient was ready to go home. Further symptoms then developed and the spleen was found to be three fingerbreadths below the costal

margin. We thought that perhaps plasmochin compound would be better than quinine, and the child was put on a regimen of one tablet a day and sent home. By the last of December the spleen was no longer palpable. At the time of last examination the red cells were practically normal and there were no parasites to be seen.

UROLOGY IN CHILDREN. H. L. KRETSCHMER.

CASE 1: *Patent Urachus.*—I. C., aged 5 months, was admitted to the Presbyterian Hospital on Nov. 11, 1929.

According to the history, urine had been passed from the navel since birth, at which time there was found a defect in the abdominal wall, through which the intestines, so-called, protruded. Three fingers could be admitted as far as the spine. There was bleeding from the navel until the beginning of the fourth week. The patient also passed some of the urine through the urethra. Since birth there had been noted a shortening of the left leg.

General physical examination pertaining to the head, neck and chest was normal. Examination of the abdomen showed the liver slightly below the costal margin. The spleen was not palpated. At the umbilicus there was a roset-like area of the skin, 2 cm. in width, from the center of which urine exuded. The left leg, by acutal measurement, was 1 inch (2.5 cm.) shorter than the right.

On cystoscopic examination the bladder appeared normal. An opening was noted in the superior wall just behind the air bubble. It was smooth and sharply defined. There were inflammatory changes around it.

A roentgenogram of the left femur showed what was probably an old fracture through the middle third with some callus formation and some shortening. The roentgenograms of the genito-urinary tract for stone were negative. A cystogram was made in the hope that the course of the patent urachus could be demonstrated. Such, however, was not the case, except for a questionable shadow at the apex of the bladder running outward toward the bladder wall on the lateral view. The blood count was normal.

The patient was operated on, Nov. 18, 1929, and the patent urachus was resected, the bladder closed in two layers, and a pezzar catheter inserted for drainage through the urethra. At the time of operation it was found that the bladder wall was much hypertrophied. There was no obstruction at the internal urethral orifice.

Two days after the operation the patient seemed to have some spasms of the bladder. Her temperature averaged 100 F. for one week prior to operation. Following the operation the temperature on the same day went to 103.6 F. The day before the patient died the temperature went to 107.4 F.

On November 24, or six days after the operation, the child began to have a diarrhea, having on this day twenty bowel movements, all very watery. The physical examination gave normal results. The diarrhea persisted for three more days.

The child died on November 27, three days after the onset of the severe diarrhea, and six days after operation

Autopsy showed an acute cystitis, acute mucopurulent bronchitis, hypostatic bronchopneumonia, and severe, acute enteritis and colitis.

CASE 2: *Hypospadias; adenonyosarcoma (bilateral).*—J. B., aged 1 year, was admitted to the Presbyterian Hospital on July 17, 1929, and was in the hospital for four weeks.

The previous history was unimportant. The complaints on admission were the presence of enlargement of the abdomen and a tumor mass on the right side.

The child was a full term, normal baby who had been in perfect health up to the time of admission to the hospital. Six weeks before admission the mother was bathing the child and she asked her mother-in-law if the child's abdomen was not too large. The mother-in-law felt the abdomen and noticed a hard, nodular mass in the right hypochondrium. The parents called particular atten-

tion to the facts that the mass was not painful, that it had gradually increased in size until the last two weeks, when it grew very rapidly, extending from the costal margin to the crest of the ilium. There were no urinary symptoms nor any history of blood in the urine. There was some difficulty in the urinary stream, due to the fact that the patient had hypospadias. The urethral opening was found at the junction of the penis with the scrotum.

The general physical examination gave normal results for the observations in the abdomen. The abdomen was prominent on the right side and there was definite enlargement of the superficial veins of the abdomen, both right and left, more marked on the left side; no rigidity or tenderness was noted. A visible tumor was seen in the right upper quadrant. The mass extended from the arch of the rib down to the crest of the ilium and two and one half fingerbreadths beyond the left of the umbilicus. The border was easily palpable. The mass was firm and smooth, felt quite elastic and was freely movable. The external genitalia were normal except for the presence of hypospadias.

Examination of the blood showed 16,200 white cells.

Roentgen examination showed a uniform dense shadow over the right half of the abdomen. A pyelogram of the left side showed a normal kidney and pelvis; one of the right side showed the ureter displaced to the left side of the abdomen, apparently having been displaced beyond the midline by a large tumor. A pyelogram was made, but no fluid reached the pelvis of the kidney. An injection of barium sulphate showed the right half of the colon displaced to the midline. Examination of the urine gave negative results.

The Wassermann test of the blood gave negative results. Blood chemistry before operation showed: urea nitrogen, 23.4; uric acid, 5.0; creatinine, 22; total nonprotein nitrogen, 41.7.

On July 21, 1929, a right nephrectomy was done. Histologic sections showed adenomyosarcoma. Following the operation some suppression of urine developed. Examination with a catheter showed the bladder to be empty. Coincident with this lack of urinary secretion the left kidney was enlarged. Cystoscopy was performed; an indwelling catheter was inserted in the ureter, and a prompt flow of clear urine was obtained. The catheter was removed. Two days later the patient again passed no urine and again the left kidney was larger.

A chemical analysis of the blood taken on July 26 showed: urea nitrogen, 100; uric acid, 9.1; creatinine, 4.3; total nonprotein nitrogen, 155. With the rapid rise in the chemical constituents of the blood and because of the anuria it was decided to perform a decapulation of the remaining kidney. This was done July 29, 1929. At operation the kidney was found to be normal. There was no hydronephrosis and no dilatation of the pelvis; the ureter and the vascular pedicle were normal.

Following this the child secreted a good deal of urine which came out through the drainage tube; also voided through the urethra.

August 5, or six days after the operation, the urea nitrogen dropped down from 133 to 29.1. The child made an uneventful recovery and was discharged Aug. 20, 1929.

A second admission occurred on September 23, five weeks after leaving the hospital, with the statement that the child was normal, that he passed his urine and that everything was all right until one week before; at that time urine was not passed through the urethra but was discharged through the fistulous opening. Two weeks before readmission a tumor mass was seen beginning under the left costal margin. On examination this mass appeared to be about the size of a large fist.

A second operation was performed on Sepember 24. The observations were: a tumor the size of a peach, and another tumor adherent to the kidney. Sections showed adenomyosarcoma.

The patient left the hospital Oct. 18, 1929, and died soon afterward.

Case 3: L. MacA., at the age of 3 weeks, was admitted to the Presbyterian Hospital on the service of Dr. Grulee.

The complaints were jaundice, refusal to eat and continual crying. At the end of the first week of life when the red color began to clear, the child appeared yellow. The mother consulted a doctor and was told that this condition would clear up.

Physical examination showed the liver dulness to be high, extending up to the fourth interspace. The heart and lungs were normal. The liver margin extended 2 cm. below the costal margin. The external genitalia were normal.

Examination of the urine showed the presence of a large amount of pus: 2,000 pus cells per cubic millimeter. The Wassermann reaction of the blood and Kahn's test gave negative results. Gold chloride showed 1121000000. Wassermann tests of the blood were repeated three or four times and were always negative.

The child ran an exceedingly septic course of temperature that averaged 102 F. Because of the fever and the persistent pyuria, it was decided to subject this patient to genito-urinary examination. Roentgenograms were negative for stone in the urinary tract. A cystoscopy on May 12, 1927, showed the bladder and the left ureter to be normal; the right ureter appeared normal.

An operation was performed on May 28, 1927.

The child was discharged from the hospital June 14, 1927, and made an uneventful recovery.

DEMONSTRATIONS OF INTRAPERITONEAL THERAPY IN CHILDREN. HEYWORTH N. SANFORD AND E. S. WATSON.

Intraperitoneal therapy offers a rapid and safe means of introducing substances into the child's body when the small size of the veins makes intravenous administration difficult and dangerous:

1. Intraperitoneal arsphenamine. Fifty milligrams of neoarsphenamine are dissolved in 5 cc. of sterile water and given intraperitoneally. The usual course of treatment is two injections every week for four weeks, and then one injection a week for four weeks. This usually results in a clearing of the Wassermann reaction. Occasionally a repeating course is necessary. This method has been used for five years and appears to give permanent results.

2. Intraperitoneal iron. Eight milligrams of collodial iron in a 5 cc. solution is given intraperitoneally twice a week for four weeks. There is a slow but steady rise in hemoglobin after two weeks. The best results are obtained by giving one or two intraperitoneal injections of whole typed blood in conjunction with the iron. The blood acts on the hemoglobin at once, and as its effects are beginning to wear off, the iron begins to take effect. This is used in cases of secondary anemia in children, particularly those due to infection and malnutrition.

3. Intraperitoneal dextrose. The dextrose is prepared in our laboratory by sterilizing 5 Gm. in Pyrex tubes by pressure. This is added to 100 cc. of sterile water just before using. By this method all of the unfortunate results obtained by the formation of an acid solution are obviated. The solution is given with a 100 cc. Luer syringe and a no. 18 gauge needle into the middle of the right rectal sheath, under sterile conditions. It may be given five or six times a day and as long as necessary. It is indicated in all cases of dehydration, such as intoxications, infections and lobar pneumonia.

A CASE OF INTRAVENTRICULAR HEMORRHAGE. DR. GRULEE.

This baby was premature, blue at birth, and had to be resuscitated. There was evidence of increasing circumference of the head. A needle inserted into the ventricle gave pure blood, the cells being crenated. The conclusion was that the child had survived an intraventricular hemorrhage with rupture and blood in the spinal canal. A roentgenogram showed definite separation of the sutures. The question arises whether the continued enlargement of the head was due to hemorrhage, or to the drainage being shut off. Dextrose had been administered intraperitoneally.

CONGENITAL HEART LESION (?). DR. MARIAN CRANE.

A boy, aged 3 years, was said to have had a normal birth, but the mother was uncertain as to whether he was blue following birth. He had twenty-seven convulsions within one week, and at that time a blue tinge developed which persisted. A few weeks later he had pneumonia, whooping-cough and measles. There had been no illnesses since then but the cyanosis had persisted, practically without change.

He was admitted to the hospital for observation on July 24, 1929. Inspection showed a well nourished, well developed boy, who was not acutely ill. The chief symptom was cyanosis, and the sclerae showed a bluish tinge. Examination showed that the teeth, particularly the incisors, were worn down to the gum margin. The chest seemed emphysematous. The lungs were clear to percussion and auscultation. The cardiac dulness was not increased. The heart rate was rapid, usually about 130; on the day of presentation it was from 140 to 180. The heart sounds were clear. There were no murmurs, but a suggestion of a thrill at the apex. The spleen was not palpable, but the liver was palpable below the costal margin. There was marked clubbing of the fingers and toes.

The laboratory observations were: At his last admission the hemoglobin was from 94 to 100 per cent. The red cells constantly numbered approximately 9,000,000. The white cells which had been 18,900 dropped to 9,800 three weeks later. The differential count showed nothing unusual. In the first smear 2 nucleated red cells were seen. Clotting time was 4½ minutes and bleeding time 2½ minutes. Neither of the child's parents showed increase in the red cells or hemoglobin. The fragility test showed slightly increased resistance to low concentrations of saline solution.

Urinalysis gave normal results except on admission when 50 white cells per cubic millimeter were found. On two occasions there was a trace of bile in the urine. The serum calcium was 11.7 per cent.

Roentgenologic observations: The lungs showed marked mottling throughout the entire field, suggestive of tuberculosis, but the Pirquet test had been negative on two occasions. The left border of the heart was very straight, suggestive of auricular hypertrophy. Electrocardiograms showed nothing definite.

The only explanation for the observations is the probability of a congenital heart lesion.

THYROTOXICOSIS (?). DR. E. S. WATSON.

A colored girl, aged 5 years, entered the hospital on Oct. 2, 1929. She complained of vomiting, loss of weight, night sweats, listlessness and nervousness, all of five months' duration. She was the result of a cesarean delivery. No abnormality was noted at birth. She was nursed until she was 17 or 18 months of age. She talked and walked at about 17 months. Two other children are living and well and there is no hereditary disease of note. There is a history of thyroid disturbance in the family.

Physical examination on entrance showed her to be poorly nourished, with definite exophthalmos, thyroid enlargement chiefly to the right, with a definite bruit, cardiac hypertrophy with a mitral lesion, infected teeth and tonsils, ankle clonus and secondary anemia.

The Pirquet and Wassermann tests were negative. Roentgenologic examination showed the heart definitely enlarged, especially the ventricle and auricle, on the right side. The basal metabolic rate, according to the Dubois standard, was +18. Helmholz has said that these rates are markedly inaccurate.

Because of the bad condition of the teeth and the possibility that there might to be an infective process, the tonsils were removed on October 11. Following this the patient had a typical thyroid crisis, and four ampules of digifolin were given in the next twenty-four hours, but had no effect on the pulse. The administration of compound solution of iodine was started, and within twelve hours the pulse

rate decreased; she ate without nausea or vomiting and improved clinically. She was kept on compound solution of iodine for about two weeks and the pulse rate was reduced to about 100. The digitalis was discontinued but the pulse rate did not increase.

The basal metabolic rate was then —1.

She was taken to the operating room for the removal of the thyroid gland, but under the anesthetic she went into collapse, so only a double ligation was performed and a piece of the gland was removed for study. It showed definite hyperplasia, which is characteristic of this type of thyroid.

Following the operation, 30 minims (1.8 cc.) of compound solution of iodine was given in the first twelve hours. She was sent home after recovery from this and was supposed to be kept at rest. She was not, and she returned to us three weeks prior to presentation in as bad condition as before. A second course of iodine was started and she immediately improved. At the time of presentation she was in such good condition that further surgery was considered.

ANEMIA WITH PECULIAR BONE CHANGES IN THE SKULL. DR. A. H. PARMELEE.

During the past summer there were two patients with severe anemia in the Presbyterian Hospital who attracted considerable attention on account of unusual bone changes in the skull and on account of their mongoloid appearance. Both were Italian, and 4 years of age, one a boy and the other a girl.

This boy was admitted on September 5 on account of pallor and weakness of two years' duration. He was normal at birth, breast fed for four months and then given condensed milk. No cod liver oil was given. Development was said to be normal and aside from grip at 1 year of age and a few colds he had not been sick. The family history was unimportant. At two years it was noticed that he was pale, tired very easily and was not disposed to play with other children. He had one transfusion of blood at another hospital a few months before coming here and his mother thought that he had improved somewhat. He had had no nosebleeds.

He was rather poorly nourished and his mucous membranes were very pale. His skin had a yellowish bronzed appearance, probably accentuated by his auburn hair. His head appeared large with increased prominence of parietal and frontal bosses. The face appeared mongoloid because the epicanthal folds were accentuated by high thick zygomas. The whole maxilla looked full and thick. His teeth and tonsils were in a poor condition. The heart was enlarged; a systolic murmur was heard over the entire precordium, and a bruit over the carotids. The liver and spleen were enlarged and hard. No ecchymoses or edema were found. The Wassermann and Kahn tests were negative. The Pirquet reaction was negative. The chemical analysis of the blood gave normal results: calcium 9.8, and phosphorus 5.6. The cultures of the blood were sterile.

The blood picture showed: red blood cells, 2,120,000; white blood cells, 12,000; hemoglobin, 30; platelets, 120,000; polymorphonuclears, 50; small mononuclears, 45; large mononuclears, 4; eosinophils, 1. Marked anisocytosis and poikilocytosis were present. There were no sickle cells. In the fragility test, hemolysis began in 0.34 per cent saline solution and was complete in 0.28 per cent; in the father's blood it began at 0.38 per cent and was complete at 0.28 per cent, and in the mother's it began at 0.32 per cent and was complete at 0.26 per cent.

During two months in the hospital the hemoglobin gradually increased to 40, and the red blood cells to 3,460,000, while the white blood cells fluctuated from 9,000 to 12,000; 1 or 2 nucleated red blood cells were found on a few counts, and once 4 reticulocytes were counted in an examination of 1,000 red blood cells. During the first two weeks, the patient's temperature was from 99 to 101 F., after which it remained nearly normal. Twice he was given, intraperitoneally, 200 cc. of his father's blood citrated. He also received cod liver oil and viosterol.

Roentgen observations were: The cranial bones were much thickened; there was a definite raylike arrangement of the thickened cortex of the entire skull

vault, most marked over each frontal bone. The long bones were rarefied and had some fine transverse lines giving them a marble-like appearance.

The changes seen in the skull bones were similiar to those described by Cooley in a group of severe anemias. Similar changes in localized areas of the skull had been described by several authors, notably Cushing and Phemister, as occurring over a meningo-endotheliomas.

Evidently hyperostosis of this type may be caused by local stimulation from an adjacent tumor which invades the bone, and also by a systemic disease which causes stimulation of the erythroblastic tissues to the point of exhaustion and hyperactivity of bone production. Dr. Schultz of Michael Reese Hospital described accurately the pathology of the hyperostoses in a similar case, cited by Cooley.

Book Reviews

THE MEASUREMENT OF NERVOUS HABITS IN NORMAL CHILDREN. By WILLARD C. OLSON, PH.D. Price, $2. Pp. 125. Minneapolis: University of Minnesota Press, 1929.

The writings on what is called nervousness are in a state of confusion and uncertainty. The clinical conception of neuropathic diathesis is unclear, not to say inaccurate. The psychologic theories that attempt to explain the mechanism of "these most common functional disorders" are built on a bed of sand. Not until there are attempts to study this group of diseases by experimental methods of physiology and psychology and to interpret the data through careful statistical analysis can one hope for a more lucid, permanent basis for the diagnosis and treatment of "nervousness."

Dr. Olson has made such an attempt in this monograph. He has tried to study one phase of the subject from the ground up — the normal child — and although he has not answered many important questions or given the pediatrists much aid in the diagnosis and treatment of this group of disorders, he has done what must necessarily be done first in order to understand any disease — he has started from the beginning. In his study he presents: (1) the critera of so-called nervous habits, in normal children. (2) He tries to determine the origin and incidence of tics. (3) He attempts to establish tests and measures for the diagnosis of tics. In chapters I and II, the author makes an inventory of the whole subject of tics with reference to the definitions and etiology. He believes that a habit spasm is produced by a physical cause and that a tic is a manifestation of a neuropathic predisposition associated with a mental process. This is an arbitrary distinction, which is not agreed to by all authorities. Chapter III is devoted to a discussion of his technic of observation. He found that during ten minute periods of observation, as they sat in their seats in school, 29 per cent of boys and 45 per cent of normal girls of primary grades were subject to one form of tic or another. The reviewer questions his right to call any penetration of the mouth by thumb or fingers a tic.

A study was also made on rats: Applications of collodion were made to the ears of two animals. Two other animals were used as controls. The rats treated experimentally showed many more removing and cleaning movements than those used as controls. Even after the experiment had been stopped, the contrast between the two groups was quite noticeable. Among the most important conclusions are: (1) A relationship exists between the amount of nervous habits and age. (2) Fatigue during the school day tends to increase the number of nervous habits. (3) The underweight child has more nervous habits than the normal child at all ages.

This monograph can be recommended to the pediatrist as a careful, concise, preliminary, objective study of this important subject.

COUGH IN INFANTS. By P. GAUTIER. Paper. Price, 18 francs. Pp. 173. Paris: L'Expansion Scientifique Française, 1930.

The physiology of the cough reflex is discussed, then the different causes of cough. The conditions are divided into cough from the respiratory organs, infectious diseases, cardiac cough and cough of the new-born infant. The diagnosis of these conditions from the type and character of the cough is then given. The treatment is directed to the cause and is similar to the American method of treatment.

Directory of Pediatric Societies

INTERNATIONAL

International Pediatric Congress

Prof. I. Jundell, Artillerigatan 23, Stockholm, Sweden.
Place: Stockholm. Time: Aug. 17-20, 1930.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. William Weston, 1231 Bull. St., Columbia, S. C.
Secretary: Dr. C. A. Aldrich, 545 Lincoln Ave., Winnetka, Ill.
Place: Detroit. Time: June 23-27, 1930.

American Child Health Association

President: Hon. Herbert Hoover, 370 7th Ave., New York.
Secretary: Dr. Philip Van Ingen, 370 7th Ave., New York.

American Pediatric Society

President: Dr. Joseph Brennemann, 30 N. Michigan Blvd., Chicago.
Secretary-Treasurer: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Place: Windsor Hotel, Montreal. Time: June 17-19, 1930.

Association of American Teachers of the Diseases of Children

President: Dr. Lawrence T. Royster, State Board of Health, University, Va.
Secretary: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Place: Detroit. Time: June 24, 1930.

Children's Hospital Association of America

President: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Secretary-Treasurer: Miss Bena M. Henderson, Milwaukee Children's Hospital, Milwaukee.
Place: New Orleans, La. Time: October, 1930.

Canadian Society for the Study of Diseases of Children

President: Dr. E. A. Morgan, 160 Bloor St., Toronto, Ont.
Secretary-Treasurer: Dr. George E. Smith, 244 Bloor St., W., Toronto, Ont.
Place: Brockville, Ont. Time: June 20-21, 1930.

SECTIONAL

Central States Pediatric Society

President: Dr. Edward Clay Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary: Dr. A. H. Parmelee, 310 S. Michigan Blvd., Chicago.
Place: Memphis, Tenn. Time: Fall, 1930.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. H. Leslie Moore, 1717 Pacific Ave., Dallas, Texas.
Secretary: Dr. Ludo von Meysenbug, 3501 Prytania St., New Orleans, La.
Place: Louisville, Ky.: November, 1930.

STATE

Alabama Pediatric Society

President: Dr. Hughes Kennedy, Jr., Highland Plaza Apts., Birmingham.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22nd St., Birmingham.

Georgia Pediatric Society

President: Dr. W. N. Adkins, Medical Arts Bldg., Atlanta.
Secretary-Treasurer: Dr. E. N. Gleaton, 212 E. Gaston St., Savannah.

Louisiana State Pediatric Society

President: Dr. J. A. Crawford, Lake Charles.
Secretary-Treasurer: Dr. C. T. Williams, 7401 Burthe St., New Orleans.

Oklahoma State Pediatric Society

President: Dr. William M. Taylor, Osler Bldg., Oklahoma City.
Secretary: Dr. Carol Pounders, 110 W. 10th St., Oklahoma City.
Place: Shawnee. Time: May, 1930.

South Carolina Pediatric Society

President: Dr. M. W. Beach, 126 Meeting St., Charleston.
Secretary-Treasurer: Dr. Julian P. Price, The McLeod Infirmary, Florence.

Texas Pediatric Society

President: Dr. H. P. Ledford, 1310 9th St., Wichita.
Secretary-Treasurer: Dr. John G. Young, 3930 McKinney Ave., Dallas.

Virginia Pediatric Society

President: Dr. Franklin D. Wilson, 136 York St., Norfolk.
Secretary: Dr. J. B. Stone, 2042 Park Ave., Richmond.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. John Toomey, Cleveland City Hospital, Cleveland.
Secretary: Dr. A. B. Grossman, 7016 Euclid Ave., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Secretary: Dr. Lawrence Murray, 1870 Bloor St., West, Toronto.
Time: November 17, December 15, February 16 and March 15.

Bronx Pediatric Society

President: Dr. David I. Frey, 2065 Grand Concourse, New York.
Secretary: Dr. H. M. Eisenoff, 1018 E. 163rd St., New York.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

Brooklyn Pediatric Society

President: Dr. Joseph F. Paulonis, 1357 Bushwick Ave., Brooklyn.
Secretary: Dr. Irwin Schiff, 658 Eastern Parkway, Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

Chicago Pediatric Society

President: Dr. Arthur H. Parmelee, 310 S. Michigan Blvd., Chicago.
Secretary: Dr. Bert I. Beverly, 130 S. Oak Park Ave., Oak Park, Ill.
Place: City Club. Time: Third Tuesday of each month.

Detroit Pediatric Society

President: Dr. Wyman C. C. Cole, 2970 W. Grand Blvd., Detroit.
Secretary: Dr. Charles A. Wilson, 71 E. Perry St., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Secretary: Dr. William Kiser, Medical Arts Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

Memphis Pediatric Society

President: Dr. G. J. Levy, 899 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. R. Graves, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. M. G. Peterman, 167 17th St., Milwaukee.
Secretary: Dr. F. R. Janney, 418 E. North Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

Nebraska Pediatric Society

President: Dr. H. B. Hamilton, 434 Aquila Court Bldg., Omaha.
Secretary: Dr. George L. Clark, 1817 Vinton St., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive, 6 p. m.

New England Pediatric Society

President: Dr. Grover F. Powers, New Haven, Conn.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: October, January and March.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. F. Elmer Johnson, 300 West End Ave., New York.
Secretary: Dr. Hugh Chaplin, 39 E. 75th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

North Pacific Pediatric Society

President: Dr. W. F. Patrick, Medical Arts Bldg., Portland, Ore.
Secretary: Dr. L. Howard Smith, Medical Arts Bldg., Portland, Ore.

Northern California Pediatric Society

President: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

Northwestern Pediatric Society

President: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Secretary: Dr. F. G. Hedenstrom, 218 Lowry Bldg., St. Paul.
Place: University Campus and Rochester, Minn. Time: Winter, Spring, Summer, Fall.

Philadelphia Pediatric Society

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. David H. Boyd, 200, 9th St., Pittsburgh.
Secretary: Dr. Theodore O. Elterich, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. Basil B. Jones, 2618 Grove Ave., Richmond, Va.
Secretary-Treasurer: Dr. John S. Weitzel, 3103 W. Franklin St., Richmond, Va.
Place: Westmoreland Club, 601 E. Grace St. Time: First Thursday of each month (other than during the summer).

Rochester Pediatric Society

President: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Howard F. Rowley, 278 Alexander St., Rochester, N. Y.
Place: Arranged by program committee. Time: First Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. Elsie Seelye Pratt, Republic Bldg., Denver.
Secretary-Treasurer: Dr. Wilford W. Barber, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month from September to May, inclusive, 2:30 p. m.

St. Louis Pediatric Society

President: Dr. Park J. White, Beaumont Bldg., St. Louis.
Secretary-Treasurer: Dr. Ralph L. Cook, 508 N. Grand Blvd., St. Louis.
Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

Seattle Pediatric Society

President: Dr. Vernon W. Spickard, Cobb Bldg., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. William S. Bowers, 1136 W. 6th St., Los Angeles.
Secretary: Dr. Fred L. Glascock, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. W. D. Lyon, 101 S. Balch St., Akron, Ohio.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: About November 22, 1930.

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